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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

MINISTRY OF EDUCATION. **The Health of the School Child. Report of the Chief Medical Officer of the Ministry of Education for the Years 1958 and 1959** [CHARLES, John]. pp. iii + 231, illustrated. 1960. London: H.M. Stationery Office. [10s. 6d.]

This report, now published biennially, appears for the first time in a cover of attractive coloured design. It is the last for which Sir John Charles, who has just retired, will write the introduction. The last volume was reviewed in this *Bulletin* [1959, v. 34, 599]. New chapters appear on children with disordered speech, selective examination as an alternative to periodic medical inspection and plantar warts. Sympathetic reference is made to the loss sustained by the department through the retirement of Dr. Robert WEAVER who has contributed to this volume a most valuable index of the main subjects dealt with in these reports since 1936.

The main conclusions are that "the great majority of schoolchildren were robust and healthy. They were taller, heavier and cleaner than their predecessors".

"Undernutrition in children has, for all practical purposes, ceased to be a problem." In fact, in many areas fat children outnumber the undernourished. "Only about 5 per cent. of schoolchildren contracted a notifiable infectious disease" in the two years but the non-notifiable, "especially infections of the respiratory passages and the digestive systems" caused much absence from school. Accidents are a serious menace to schoolchildren: in 1958 they caused 869 deaths at the ages 5–15. Cancer, mainly leukaemia, caused 499 deaths.

In 15 per cent. of the school entrants subjected to routine examination treatment was found to be needed. There is still great difficulty in staffing the school dental service and only about half the children who need dental treatment obtain it.

The reasons for the great disparities in different areas in the reported incidence of lesions of the skin at routine inspections are discussed and tables show the wide variations in the numbers submitted to tonsillectomy.

There are wise remarks on the importance of a common standard for the recording of defects found at medical examinations. There are interesting sections on ringworm of the feet, heart disease, lung disease, otitis media, orthopaedic defects, epilepsy, diabetes, undescended testicles, bed wetting, cross laterality and dyslexia.

Information has been collected on the incidence of smoking by schoolchildren. There is more dental caries and this is attributed to the increasing consumption of sugar in its various forms and to snacks between meals. There is a discussion on the problem of school "tuck shops." An appendix contains the report of a Ministry investigation into the value of the topical application of solutions of sodium fluoride to teeth by the KNUTSON method [*ibid.*, 1947, v. 22, 255] and the conclusion is reached that, although there was some reduction in caries compared with the controls, it was insufficient to justify the general adoption of this method of countering dental decay in children. An experimental two-year training course for dental auxiliaries of the New Zealand type and with an intake of 60 students a year has been started.

The new chapter on Speech Disorders says that there is a shortage of 123 speech therapists.

In an increasing number of areas there is a visit by the doctor to each school every term instead of every year and replacement of the intermediate routine examination of all children in the age-group by a more detailed examination of children specially selected. Full details are given in the report.

The long chapters on visual defects and on defective hearing cover a wide range of topics. There is considerable activity in the development of audiology units. The various steps taken to deal with the emotionally disturbed child are well described.

Those interested in plantar warts will find a full account of present knowledge in the chapter on the subject.

The chapter on infectious diseases records that in 1958 there were 30 outbreaks of epidemic vomiting.

There is a wise chapter on health education: in some schools a health visitor has been appointed full time for teaching duties in large schools.

There are 2,416 doctors, 1,591 dentists and 6,999 nurses working in the school health service. Many are part-time and the full-time equivalents are 948, 1,015 and 2,666. The number of children on the school rolls was 6,974,079 and the cost of the service in 1958–59 was £20,657,309.

[This report maintains the high quality of its predecessors and provides an authoritative survey of the activities of the school health service of England and Wales with valuable commentaries on its growing points.] *Allen Daley*

WORLD HEALTH ORGANIZATION. PUB. HEALTH PAPERS No. 4. **Aspects of Public Health Nursing.** 185 pp. 1961. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [8s. 6d.; $1·75; Sw.fr. 5.–.]

Throughout the world there is a shortage of trained nurses; this need will be met neither by exhortation nor by fatuous optimism. The problems of each country must be ascertained and scrutinized and then solved in the context of the probable resources. To anyone concerned with these problems of the training of nurses and the administration of nursing services the papers in the book under review will be of great interest.

The first paper, by Esther L. BROWN, discusses the general problem and points to the dual solution of ensuring that the trained nurse is freed of as many extraneous duties as possible, so that she has more time to do the things that only she has the training to do, and the consequential need for the employment of auxiliary personnel to whom many functions can be delegated. The difficulties, at present, are a lack of a basic policy of integrated nursing care and an unwillingness on the part of the nurse to delegate the carrying out of those technical procedures which the auxiliary personnel can pick up best in the shortest time, because the nurse identifies these very procedures as an essential part of her own nursing function. The need for a nursing team consisting of nurses and auxiliaries is further discussed in the second paper by Margaret MACKENZIE, who concludes her paper as follows: "The need for action is immediate. Experiments in staffing patterns and team training should be planned without delay so that effective services are provided as soon as possible."

Such an experiment carried out in Brazil is described in a paper by Ermengarda M. J. DE FARIA ALVIM. Nurses are used mainly in the organization of health facilities, in training programmes and in the supervision of all nursing activities. Direct services to the public are the responsibility of specially trained auxiliaries. The training of these auxiliaries is described in detail. Experience has proved that, in the rural areas, the auxiliary worker in many respects presents advantages over the graduate nurse; these advantages stem from the fact that the auxiliary worker is locally recruited, often lives with her family and "speaks the language of the people." The training and work of the *assistante sociale* in France is described in a paper by Yvonne TURPIN and the *feldshers* in the U.S.S.R. by E. D. ASHURKOV, A. ZHUK and Y. LISITSIN.

The training of the nurse with particular reference to the integration of the public health and social aspects of medical care into the basic course is discussed by Doris S. BROWN and Margaret S. TAYLOR, who give full details of the instruction at the University of California School of Nursing. Glete DE ALCÁNTARA describes the basic programme of the Ribeirão Prêto School of Nursing, Brazil, and Louise M. BELL the course at the University College Hospital, Ibadan, Nigeria. All three of these papers should be read in full.

Other aspects of public health nursing discussed in this book are the problems that nurses trained in one country face when working in another (Margaret READ), the role of the midwife in public health (Audrey WOOD), the public health nurse and administration (H. FINER), and there are two excellent papers about the nurse's responsibility for health teaching (by Margaret L. SHETLAND and Amelia M. MAGLACAS, and by Marion MURPHY respectively). The authors of the first of these two papers point out that the acquisition and subsequent display of knowledge is, in itself, insufficient. The nurse must be able to distinguish between health practices that need to be changed and practices that are not really of importance. She must also have the confidence of those she wishes to advise, and she must understand and have sympathy with the cultural habits and beliefs of the people. *M. D. Warren*

VITAL STATISTICS

SHARMA, H. R. **Birth and Death Rates in India (1951–57).** *Indian J. Med. Res.* 1961, Jan., v. 49, No. 1, 158–71.

The registration of births and deaths in India is defective. During the present century the estimated birth rate has been about 25% higher and the estimated death rate about 30% higher than the registered rate. The amount of under-registration varies widely between States and between the towns. The estimated rates are derived from 3 sources (1) the demonstration Health Units, which cover populations of 50,000–70,000 persons and the registration of births and deaths is closely supervised, (2) from sampling verification of the census by the census actuary and (3) from sampling surveys. For the States the birth and death rates by the 3 methods for each year from 1951 to 1957 has been compared with the registered rate. The author discusses the variations between these estimates and produces a single value for some States. The registered infant mortality varies considerably between the States but is far below the actual level. The proportion of infant deaths to

total deaths varies from one-quarter to one-third in the various States but is fairly constant in the same States over a period of years. For each of the States for each of the 7 years the adjusted infant mortality has been found. *W. J. Martin*

STAHLIE, T. D. **Child Mortality in Thailand.** *Trop. & Geograph. Med.* Amsterdam. 1960, Dec., v. 12, No. 4, 327–38, 3 figs.

Registration of births and deaths in Thailand has been compulsory since 1909 but the reporting system is not efficient. Births have been under-reported and the recorded rate represents only about two-thirds of the true rate; by 1954 the registration had become more reliable. Stillbirths and deaths in the first few days of life are grossly under-reported. The official stillbirth rate is 1·5 per 1,000 compared with the author's estimate of 14·5 which is still a very low rate. The infant mortality in 1955 was 56·1 per 1000 but the author estimates that the true value was 25% higher. The low infant mortality figure was due to the failure to report deaths in the first days of life; only 3% of the infant deaths were reported to have occurred during the first day of life compared with one-third in Western countries. The causes of infant deaths cannot be specified with any accuracy, tetanus neonatorum still plays an important part. There is evidence that infant mortality is decreasing rapidly and an important, if indirect, factor of this decrease is the eradication of malaria. Drowning is the chief source of accidental death and at ages under 5 drowning accounts for 84% of accidental deaths.
W. J. Martin

EPIDEMIOLOGY

ENTERLINE, P. E. & CAPT, Katherine G. **A Validation of Information provided by Household Respondents in Health Surveys.** *Amer. J. Pub. Health.* 1959, Feb., v. 49, No. 2, 205–12.

This paper is one of a growing number of studies which reflect the current concern with the effects of methods on results in health surveys. Previous surveys had shown that persons reported more disease for themselves than they reported for others [this *Bulletin*, 1957, v. 32, 638, 1128]. Adult males are the persons least likely to be found at home by interviewers and therefore most likely to be answered for by another respondent. An experimental design was therefore carried out in connexion with a health survey in North Dakota during 1956. The enquiry was undertaken by the U.S. Bureau of the Census for the Heart Disease Control Program of the U.S. Public Health Service.

The population studied consisted of males aged 35 and over. Half of them were called upon until they were found at home and interviewed personally about their health. The other half were not seen by an interviewer but an eligible adult respondent answered questions concerning them and a questionnaire was left which the adult males were asked to complete and return.

A comparison showed that there was no significant difference in the number of diseases or broad disease categories reported in the two samples. Nor were there differences in fairly objective type questions on age, height and weight. The authors, therefore, conclude that in surveys designed to measure the prevalance of major disease categories, the cheaper method of interviewing eligible respondents and leaving questionnaires is likely to yield about the same level of reporting as interviewing adult males about themselves. On the other hand, there were significant differences in the dietary information obtained by the two methods. However, other independent evidence suggests that wives may be more accurate assessors of the fat content of their husbands' diets than are the men themselves.
M. Jefferys

CHRONIC CARDIO-RESPIRATORY DISEASES

BOYADJIAN, N. Le dépistage des cardiopathies dans la population scolaire de Bruxelles. **[Detection of Heart Diseases in Schoolchildren in Brussels]** *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1960, Oct., v. 18, No. 8, 557–66.

In the Health Centre, Brussels, there has been for 2 years a cardiological section, by means of which all the schoolchildren in the city (5–18 years of age) had one thorough cardiac examination, including history, clinical findings, radioscopy, electrocardiography, and phonocardiography. The importance of such a comprehensive study is: (1) to see that parents know of the mode of life appropriate to the affected child, (2) to secure operative intervention at the ideal age in congenital heart disease, (3) to correct erroneous diagnoses of heart disease, and (4) to guide affected pupils before the age of 12 years to take up the kind of studies which will be most useful to them in the way of life which they ought to follow. These objects were fulfilled. Acquired heart disease, in other investigations more common than congenital, was found to be less common at school age than

congenital lesions in this series: diagnosis of congenital disease has improved, as has treatment of rheumatism. Organic heart disease was found in 3 to 10 per 1,000 of the schoolchildren. *H. Stanley Banks*

THOMAS, Caroline B. **Characteristics of Smokers compared with Nonsmokers in a Population of Healthy Young Adults, including Observations on Family History, Blood Pressure, Heart Rate, Body Weight, Cholesterol and Certain Psychologic Traits.** *Ann. Intern. Med.* 1960, Oct., v. 53, No. 4, 697–718. [21 refs.]

Students entering Johns Hopkins Medical School between 1948 and 1957 were asked for details of their smoking habits, as part of a long-term study of the precursors of hypertension and coronary thrombosis. Altogether 787 students were registered in the 10 years; 749 volunteered to take part in the study and information about smoking habits was obtained for 657 (597 men and 60 women). Approximately half were non-smokers (including occasional smokers) and half were regular smokers; the small proportion of former smokers (4·7%) was excluded from the present study.

Smokers and non-smokers were broadly alike in most of the characteristics examined, but several significant differences were recorded. As a group, smokers (i) more often gave a history that their parents had hypertension; (ii) had higher recumbent values for heart rate and pulse rate, but lower values for diastolic pressure; (iii) had higher serum cholesterol levels; (iv) contained a larger proportion of heavy individuals, and (v) more often reported anger and an urge to eat when under stress, and less often reported decreased activity.

No significant differences were found between smokers and non-smokers in (i) responses of blood pressure and heart rate to either the cold pressor test, an exercise test or the ballistocardiographic smoking test; (ii) academic excellence, or (iii) most of the Rorschach variables examined.

Similar differences in serum cholesterol between smokers and non-smokers and broadly similar differences in blood pressure levels have been reported for men aged 20–59 years in Finland [KARVONEN *et al.*, 1959, v. 34, 766]. It seems probable, therefore, that these differences are real.

On present evidence it is impossible to say whether the differences between the groups are genetic in origin or represent an effect of smoking. The difference in the parental histories suggests that some of the variations may be genetic. The distribution curves of all the characteristics show much overlapping between the groups and if the differences are genetic they are unlikely to be due to single genes. *Richard Doll*

See also p. 522, CORNWALL & RAFFLE, **Bronchitis-Sickness Absence in London Transport.**

CANCER

MINISTÈRE DE LA SANTÉ PUBLIQUE. Paris. Le cancer au Moyen-Orient (Israël et Iran). Données épidémiologiques [**Epidemiological Data on Cancer in Israel and Iran**] [LAURENT, C. & LEGUERINAIS, J., with the collaboration of L. MAUJOL]. *Monographie de l'Institut National d'Hygiène No. 19.* 137 pp., 2 maps & 23 graphs. [Refs. in footnotes.] 1960. Paris (16e): Inst. Nat. Hyg., 3, rue Léon-Bonnat. [13 NF.]

(*i*) *Israel*

An account is given of the different types of population now to be found in the State of Israel and the methods of medical care and cancer diagnosis. Malignant neoplasms represent 15% of all deaths in Israel, compared with 39% due to cardiovascular diseases and 9% due to deaths in the first year of life. Cancer of the stomach is the most common cause of death due to neoplasia when both sexes are combined (13%) and is found mainly in those aged more than 55 years. In men the most common cancer is that of the lung, while in women the commonest site is the breast. Cancer of the uterine cervix is one of the rarest forms (0·4%); cancer of the skin is also much rarer than in neighbouring countries, such as Iran (1·3% of all cases of cancer in both sexes).

A cancer registry was first started in Israel in 1954 and probably accounted for about three-quarters of all cases of cancer diagnosed in the country; a new scheme, similar to that in operation in Norway was started in 1960, a full account of this is given.

(*ii*) *Iran*

A similar account of the general population characteristics are given for Iran. In contrast to Western countries and to Israel cancer is only in 8th place as a cause of death, representing 3·6% of all deaths. From the available data it is not possible to define the site of the cancer. Cancer morbidity studies are somewhat incomplete, but from hospital reports in Teheran an incidence rate of 142 new cases per 100,000 population (compared with 300–350 new cases reported per 100,000 inhabitants in Europe and the U.S.A.) has been reported. Of 2,558 cases reported in the period 21/3/55 to 20/3/56 34·7% were due to cancer of the skin (excluding melanoma), 12% were due to cancer of the uterine cervix, 8·4% oesophageal tumours, 5·7% lymphosarcoma and reticulosarcoma, 4·4% Hodgkin's disease, 3·6% breast cancer. Similar distributions were found in hospital data.

[No age-standardization procedures have been used in making comparisons between the different countries.] *W. W. Holland*

KINGDON, K. H. **Possible Biological Effects of Electrically Charged Particles in Tobacco Smoke.** *Nature.* 1961, Jan. 21, v. 189, 180–82, 2 figs.

Small ions are generated by a burning cigarette, presumably by thermal ionization of potassium which is always present in substantial amounts. Generated at the burning tip, they are removed by Brownian movement and electrical forces on their way through the cigarette and do not enter the mouth. From calculation of those generated at the tip it seems likely, however, that a smoker inhales small ions at a concentration of approximately 2×10^5 ions/cc. all the time that he is smoking a cigarette. This concentration is about 1,000 times that found in an ordinary city bedroom with no smoking going on. In support of the hypothesis that it may be this inhalation which is related to lung cancer rather than any carcinogenic chemicals, 3 relevant observations are made, *viz.* (1) the cigarette is a relatively strong and continuous source of small ions whereas the cigar and pipe are not; (2) the lower parts of the bronchi will be much more readily reached by small ions than by 0·5 micron droplets; and (3) the importance of small ions would not be revealed in experiments with mice made to inhale smoke.

The hypothesis is thus advanced as an alternative approach which appears to merit further exploration.

A. Bradford Hill

SORGER, K. & MYRDEN, J. A. **Verrucous Carcinoma of the Buccal Mucosa in Tobacco-Chewers.** *Canadian Med. Ass. J.* 1960, Dec. 31, v. 83, No. 27, 1413–17, 7 figs.

Clinical and histological details are given of verrucous carcinoma of the buccal mucosa in 4 old men, each with a long history of tobacco chewing. This lesion in tobacco-chewers should be regarded as a distinct entity separated from the more usual type of oral cancer on account of its relatively benign behaviour. Local excision is the treatment of choice and tobacco chewing should be discontinued. *A. Bradford Hill*

See also p. 516, THOMAS, **Characteristics of Smokers compared with Nonsmokers in a Population of Healthy Young Adults.**

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

MÜLLER, Gertrud. Salmonellabefunde in der Elbe bei Hamburg in den Jahren 1954 bis 1959. [**Salmonella Organisms in the River Elbe at Hamburg in the Years 1954 to 1959**] *Städtehyg.* Hamburg. 1961, Feb., v. 12, No. 2, 24–7, 2 figs.

The river Elbe at Hamburg receives sewage from the main sewer which contains up to 5,000 salmonella organisms per litre. The water of the river is frequently examined bacteriologically and recorded in this paper are the details of isolations of salmonella types from a 500 cc. sample in each of the years 1954 to 1959. A table of results shows that in almost every year *Salm. paratyphi B* represented more than 50% of the total salmonella isolations, the remainder being distributed, in 1957 for example, over 20 different salmonella types the names of which are given.

The seasonal distribution of salmonella positives and the variations in the coliform titre are also recorded but whereas the latter is influenced by the temperature of the water the numbers of positive salmonella findings are more or less equally divided over the whole year.

M. E. Delafield

VOELKER, R. A., HEUKELEKIAN, H. & ORFORD, H. E. **Seasonal Coliform Variations in Well Waters.** *Amer. J. Pub. Health.* 1960, Dec., v. 50, No. 12, 1873–81, 6 figs.

A year's study of bi-weekly samples of each of 2 private house wells in New Jersey, one dug and one drilled and in different geological formations, indicated that the season of the year is an important factor in controlling the bacterial content of a well. High coliform counts were typical of the warmer months, with counts decreasing during the autumn to minimum values about January followed by a steady increase through the spring. Apparently there was a direct relationship of bacterial numbers with air temperature.

Examination of samples from 2,417 wells throughout New Jersey corroborated this seasonal trend.

[This may be a local phenomenon but is not universally experienced, as the paper seems to imply. Again, the increase may be due to coliform organisms multiplying *in situ* on packing material, etc., particularly during the warmer months; such cases have been observed in England.] *E. Windle Taylor*

McLean, D. M., Brown, J. R. & Nixon, M. C. **Microbiological and Chemical Investigations of Outdoor Public Swimming Pools.** *Canadian J. Pub. Health.* 1961, Feb., v. 52, No. 2, 61–7, 6 figs. [15 refs.]

"Regulations promulgated by the Department of Health for Ontario in 1944 prescribe that the level of free residual chlorine in pool water shall be maintained at a level not less than 0·2 parts per million (ppm.) nor greater than 0·5 ppm. in a pool in which the temperature shall be raised to a temperature not exceeding 72° F." In view of the published reports of epidemic virus diseases in users of swimming pools and the lack of information on the effectiveness of chlorine as a "virucidal" agent in swimming pools under actual operating conditions, the investigations described here were carried out at 2 outdoor pools in the City of Toronto in 1960.

The methods and materials of the study are described with a description and tables of the results which are discussed.

In the short summary of the paper it is stated that "During summer 1960 coliform organisms and other enteric bacteria were recovered from two outdoor public swimming pools in Toronto despite levels of free residual chlorine which were maintained above 0·2 ppm. No virus was isolated from 88 samples of water, possibly owing to lack of prevalence of enteroviruses in the community". *M. E. Delafield*

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

Taylor, A. H. **Sewage Lagoons for Low-Cost Disposal.** *East African Med. J.* 1960, Oct., v. 37, No. 10, 676–87, 4 figs.

In this interesting paper the Chief Health Inspector of the Kenya Ministry of Health, after a brief description of sewage-oxidation ponds, gives the design criteria adopted in the U.S.A. for these lagoons. He then describes a pair of sewage lagoons (in series) designed to treat 55,000 gallons per day of sewage from Nairobi National Airport.

These lagoons proved themselves able to handle a much higher load and satisfactorily treated BOD loads up to 250 lb. per acre per day on the primary pond. At higher loadings the lagoons became anaerobic and aerobic conditions had to be restored by recirculation of secondary-pond effluent. The lagoons caused no fly problem and mosquito control was unnecessary after the initial period; clearing is necessary in the effluent channel to control culicine breeding.

The capital cost of these lagoons was £3,500 for a BOD load of about 225 lb. per day. [This corresponds to a population load of about 1800 so that the capital cost is about £2 per head which may be compared with 20s. to 30s. for similar ponds in Israel (Personal Communication from Mr. J. L. A. Watson to the reviewer) and with £6 to £12 or more for full conventional treatment in Britain (Townend, *Proc. Inst. Civil Engineers*, 1960, v. 15, 214).]

[One comment may be offered. On p. 679 the author writes: "Negative B.O.D.s were obtained showing that the effluent was free from polluting matter". Indeed, these show no such thing, but demonstrate that the liquid under test was not under oxygen equilibrium with the atmosphere at the temperature of the test at the start of the incubation—and, possibly, that the incubation was not carried out in the dark.] *Peter C. G. Isaac*

INFESTATION

Graves, J. C. & Graves, Valerie. **Two Hundred Cases of Scabies in General Practice.** *J. College General Practitioners.* 1959, Nov., v. 2, No. 25, 380–84, 3 figs.

This is a report on an enquiry into the incidence and epidemiology of scabies, which was carried out in the Epidemic Observation Unit of the College of General Practitioners between February 1957 and August 1959. Information on 215 examples of the disease was obtained. The following points emerge:—

(i) scabies is more common in the winter months.

(ii) while in childhood there is little difference between the sexes, from 11 to 30 years of age females predominate: among elderly patients, men (usually tramps) are more frequently affected,

(iii) several areas of the body are usually affected simultaneously, only the face and scalp being spared,

(i) patients often come from clean and tidy homes,

(v) in a few instances a canine acarus is acquired from a pet dog,

(vi) response to benzyl benzoate is a useful diagnostic test and may be used successfully in atypical irritant rashes. *J. H. Walters*

ATMOSPHERIC POLLUTION

BÄUMLER, J. & MÜLLER, R. Zur Bestimmung von Autoabgasen in der Strassenluft. **[Estimation of Exhaust Gases from Motor Cars in the Air of Streets]** *Ztschr. f. Präventivmed.* Zurich. 1961, Jan.–Feb., v. 6, No. 1, 10–23, 7 figs. [15 refs.]

The English summary appended to the paper is as follows:—

"After a review of the important toxic gases from motor-cars there is a description of the methods and results of determinations in the air of streets and garages at Basle.

"Carbon monoxide, determined with the recording 'Dräger-CO-apparatus' was found in streets with great traffic in a quantity up to 0,003 V%. The concentrations in a subterranean garage were sometimes higher than 0,01 V%.

"For the sampling procedures of exhaust-gases of motor-cars (Formaldehyd, Nitrogen oxides, Ammonia, Sulfur dioxide) a transportable apparatus is described and some results of the air pollution in the streets of Basle are given."

CROSSE, P. A. E., LUCAS, D. H. & SNOWSILL, W. L. **Instrument for recording the Dust Nuisance emitted by Chimneys.** *J. Sci. Instruments.* 1961, Jan., v. 38, No. 1, 12–17, 6 figs.

This instrument is designed to measure and record the likelihood of dust emitted from a chimney causing nuisance at ground level, and is complementary to instruments which measure the optical density of flue gases and hence the nuisance of visible plumes. The collecting and measuring unit is put in a horizontal duct leading to the stack, and the sampling head faces the gas stream so that inertia carries the heavier particles into the head, where they settle on a glass plate. At set intervals the dust collected is estimated photometrically. The glass surfaces are then cleared by a blast of air, and the cycle starts again. Readings are recorded automatically. The instrument is carefully compensated so that it is unaffected by drift in the lamps or photocells or by gradual dirtying of glass surfaces.

The efficiency of a design such as this, which in effect depends on impaction for capture of particles, will clearly depend on the velocity of the gas being sampled, but the authors show that for velocities between 20 ft. per sec. and 45 ft. per sec. this dependence is not critical.

The design "is based on the assumption that vertical surfaces are more important in pollution than horizontal surfaces, and that coarse particles are more likely to cause nuisance than fine particles". The theory behind these assumptions is to be discussed in a later paper: They will not however be accepted universally, and in particular the implication that coarse particles are more important than fine on vertical surfaces seems to the reviewer to be untrue. The instrument nevertheless has interesting features, and could prove useful for sampling the coarser particles in stack gases ($> 50\mu$).

J. McK. Ellison

LUXON, S. G. **A Method for the Estimation of Particulate Atmospheric Contaminants in Trace Amounts.** *Ann. Occup. Hyg.* London. 1961, Jan., v. 3, No. 1, 30–32, 2 figs. on 2 pls.

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

INSTITUTE OF DIRECTORS. **Better Offices.** pp. 26–149, numerous illustrations. 1961. London: 10 Belgrave Square, S.W.1.

It is over 150 years since the Health and Morals of Apprentices Act provided the first legislation which developed into our modern Factory Acts. These Acts protect the health, welfare and safety of the 9 million workers employed in the manufacturing industries. It is over 10 years since the GOWERS Report made its recommendations on the health, welfare and safety of shop and office workers, besides those in certain other non-industrial occupations [this *Bulletin*, 1949, v. 24, 765]. In the last 20 years there has from time to time been political or trade union pressure for improving the conditions in which over 2 million clerks, secretaries, typists, etc., are employed. It might be interesting to speculate on the reasons which have enabled the industrial workers to receive substantial protection from the hazards of their work, while the clerical and office worker has been given no such protection. The pressures from the trade unions have clearly had a greater impact in industrial than in commercial enterprises, and perhaps, notwithstanding the slum offices and sweated

clerical workers of Dickensian England, the office worker really was much better off than his industrial counterpart.

This publication by the Institute of Directors is a glossy-covered expression of the concern felt by those engaged in management for the improvement of working conditions of this forgotten population. The magazine consists of some 130 pages of articles, and about half as much space is devoted to advertisements for office equipment, office furnishings, office machinery, etc. The articles are illustrated by admirable photographs, plans and diagrams, all of which are closely associated with the subject matter. They are grouped into 8 sections which include factual and informative discussions of internal environment (*e.g.*, heating, ventilation, lighting and noise), amenities (catering and cloakroom and washing facilities), fire and accidents, and an aspect of working conditions frequently overlooked, namely, furniture and fittings. This last section not only discusses some of the modern developments in the design of filing cabinets, office desks and seats, but also has a sub-section dealing with different types of carpets and upholstery fabrics. It seems a pity that this "Furniture" section, which makes an oblique reference to it, fails to record the current work being done in Britain under the title of Ergonomics. The section dealing with a new building, how to get it and what it will cost, would appear to be admirable in its precise factual information, but clearly the person intending to build must proceed from these two articles to the specialist for information relevant to his own particular problems.

In general, the publication is attractive, informative and full of thought-provoking ideas. It has, to the reviewer, some frustrating features. The method of indexing is inconvenient and clumsy. A glossary at the end contains most of the references as well as certain definitions and picture credits. It is difficult to see why the information about individual pictures cannot appear on the same page as the picture. References to technical journals would be more convenient if they were associated with the article to which they apply, as the reader has to look forward and backward if he is to glean all the information which is available to him. Such a criticism, however, is perhaps unfair, since this extremely attractively presented journal gives much useful information and is likely to stimulate the reader.

Coming as it does from a body as influential as the Institute of Directors, it may have more positive effect that the drier utterances of departmental reports, or the demands by workers for better working conditions.

As a final comment the reviewer notes once more that good design not only is efficient, but also, generally, looks right. *H. G. Maule*

JONES, A. R. & CHURCH, F. W. **A Criterion for Evaluation of Noise Exposures.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 481–5, 6 figs.

The authors have derived a series of "Hearing Conservation Criteria" (*i.e.* levels of exposure above which hearing conservation measures become desirable) for weekly periods of exposure ranging from 0·1 to 40 hours. The criterion for exposure of 0·1 hours per week is based broadly on an "equal energy received" concept, with an over-riding maximum of 135 db. in any octave band.

A nomogram is given, to be used in conjunction with the criteria, for use where men are exposed to several noise levels over the working period. For each type of exposure the percentage of the allowable weekly dose received is calculated. The addition of these percentages for each type of exposure will indicate whether or not the total dose received is excessive. *D. E. Hickish*

PIHL, S. E. **Evaluation of Exposures to Industrial Noise.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 486–90.

This paper reviews some of the practical considerations in making accurate and meaningful sound level measurements and octave band analyses in industry.
D. E. Hickish

VISHNEVSKAYA, S. S. & GORSHKOV, S. I. **[Certain Features of the Action of Noise in Weaving Sheds and Measures to Control them]** *Gigiena Truda i Professional'nye Zabolevaniya.* Moscow. 1960, v. 4, No. 11, 18–24. [In Russian.] English summary.

The environment in weaving sheds is warm, humid and noisy. It is a high frequency noise reaching 102–105 db., which exceeds the permissible level (80 db.) for that type of noise. [The Russian damage risk criteria are intermediate between those of ROSENBLITH and his colleagues and those of BURNS and LITTLER..]

A study of weavers subjected to this environment showed slowing of the pulse by an average of 10 beats per minute (toward the end of the working shift) together with electrocardiographic changes, indicative of the influence of the vagotonic component of the vegetative nervous system. It was found that despite there being no change, or even a lowering of the body temperature, there was a sudden rise in the skin temperature of the chest and forehead reaching 35–36° C.; this was not accompanied by a noticeable increase in sweat production. It is concluded that "the temperature of the skin as an index of the functional state of the vessels on the surface of the body reflects not only the influence of the distinctive microclimatic conditions [local environment] but also the action, on the vegetative nervous system of the workers, of other unfavourable industrial conditions of weaving sheds". This is interpreted as an increased tone of the parasympathetic component. At the same time a change in the correlation between the latent period of reaction to light and sound was observed (usually the latent period of reaction to light is greater than to sound). Audiometry was carried out on 10 weavers with a period of service of up to 5 years before and after work. Before work the auditory sensitivity was decreased by 10–25 db. at frequencies of 2,048 to 8,192 c.p.s., the greatest loss being at 4,096 c.p.s. At the end of the shift the hearing loss was about 20–35 db. [There is no note of age, or of clinical state of the hearing mechanism.]

Because of the number of factors operating (noise, unpleasant microclimate, nervous strain) it was decided to conduct some laboratory experiments. The subjects were 7 women, aged 20–25 years, and they were subjected to weaving shed noise of 105 db. for 3 hours in a sound chamber with an air temperature of 15–18° C. During this time they read light fiction. In the first series of experiments the ears were unprotected, in the second they were fitted with modified Czechoslovakian "inner antiphones". A table shows the alteration in 7 subjects at different frequencies; the average is 25 db. at 256, 512 and 1,024 c.p.s., 30 db. at 2,048 and 40 db. at 4,096 c.p.s.

The latent period of reaction to sound was increased on average by 58 sigma after 90 minutes exposure to noise and by 28 sigma immediately after the noise stopped. With antiphones the increase after 90 minutes was 22 in 5 subjects and a decrease of 12 in 2 subjects; immediately after the noise there was a decrease of 10 sigma in all subjects. Similar results were found in the change of latent period of reaction to light. The pulse rate showed a fall of 10 when antiphones were not worn and 5 when they were worn; the fall in pulse rate was 4 in controls (persons going into the sound chamber briefly to take the measurements—every 30 minutes). The skin temperature of the forehead rose 1·3° C. when no antiphones were worn and 0·9° C. when they were worn; corresponding figures for the chest were 1·1° C. and 0·7° C. In the control group changes of skin temperature were "hardly noticeable" and rose 0·5° C. toward the end of the experiment.

The threshold of auditory acuity was tested before and after exposure, both with and without antiphones. The table shows the results:—

Changes in auditory sensitivity

	Frequency of vibrations in seconds				
Group of subjects	256	512	1024	2048	4096
Without antiphones (first series)	+5	+5	+10	+10	+5
With antiphones (second series)	0	−5	0	−5	−5

Plus indicates dulling of the auditory acuity, minus—intensification of auditory acuity.

[This article will be of interest to all those studying the effects of loud industrial noise. The approach is quite different from that usually seen in Western medical literature.] *W. R. Lee*

ŁABA, L. & RUSZEL, J. **About Permanent Injury of the Ear in Divers.** *Bull. Inst. Marine Mer. Gdańsk.* 1960, v. 11, Nos. 3/4, 165–74, 3 charts. [13 refs.]

Laryngological and audiometric examinations were carried out in Gdansk on 49 divers, 25 to 50 years of age, who had been diving for 5 to 18 years.

9 divers suffered from acute barotraumatic inflammation of the middle ear, and 3 from decompression sickness with neurological symptoms.

Of the 45 divers under 40 years of age, 24 had normal hearing, 11 had unilateral hearing loss and 10 had bilateral hearing loss. 11 of those with hearing loss had no history of acute barotraumatic inflammation of the middle ear or decompression sickness with neurological symptoms. In all cases the observed hearing loss was at frequencies above 2,000 cycles per second. *D. E. Hickish*

FRANCO, S. C., GERL, A. J. & MURPHY, G. T. **Periodic Health Examinations: a Long Term Study, 1949–1959.** *J. Occup. Med.* Chicago. 1961, Jan., v. 3, No. 1, 13–20, 1 fig.

In 1949 the Consolidated Edison Company inaugurated annual periodic health examinations on a voluntary basis for salaried personnel, and this paper reviews the results of 10 years' experience. Participants were mainly men—fewer than a dozen women—in the age-group 40 to 65 and during the years 1949 to 1959 a total of 717 persons availed themselves of the facilities offered; in fact 70% of those eligible. The periodic examination included certain routine laboratory tests, but other specialized procedures were carried out only for specific indications, and the cost has averaged approximately 40 dollars per case per year.

In more than half (59%) of the 717 persons undergoing periodic examination, conditions of major medical significance in themselves or as precursors of potentially serious disease were noted. Of the 421 with major diseases, approximately 10% knew of conditions which they wished to have checked, but a considerable number, 36%, were entirely asymptomatic. The medical history and the physical examination accounted for nearly 60% of the diagnoses, the electrocardiogram for 20%, and the laboratory tests, X-ray procedures, and special studies for the remainder. Full details of the clinical findings are to be found in a number of tables and there is a certain amount of discussion in the text concerning the significance of these findings.

With the early detection of disease tendency in mind the authors studied the value of three special procedures: (1) the "2-step" electro-cardiogram exercise tests, (2) detection of hyperuricaemia and hypercholesteraemia, and (3) proctoscopy. They used the double standard "2-step" test described by MASTER (*Ann. Intern. Med.*, 1950, v. 32, 842) but found that his criteria for abnormal response were too inclusive and would result in the overdiagnosis of coronary disease candidates. The criteria observed in this study were based on a depression of the R-ST junction of at least 1 mm. in the limb leads, or more than 0·75 mm. in the praecordial leads, even if it is present in the one-minute tracing. After some discussion of their findings with this test the authors conclude that it cannot be used for prognostication in the individual case but it does help to delineate a group in whom there appears to be an increased incidence of coronary heart disease and may therefore indicate those persons who might benefit from health education.

No significant evidence was found in this 10-year study to support the possible value of serum uric acid and blood cholesterol determinations as predictors of degenerative cardio-vascular disease, and although the results of routine proctoscopy were not impressive the

authors feel that proctoscopy should be carried out as a routine procedure and repeated at least once within a 5-year period. [The authors found, as many others have, that persons subjected to routine annual medical examinations, develop confidence in the medical practitioner who goes to so much trouble, and tend to consult him in the interim period, at a very early stage for new complaints. This result, from such routine programmes, is probably as important as the detection of existing lesions and asymptomatic disease.]

P. J. R. Challen

CORNWALL, C. J. & RAFFLE, P. A. B. **Bronchitis-Sickness Absence in London Transport.** *Brit. J. Indust. Med.* 1961, Jan., v. 18, No. 1, 24–32, 1 fig.

This is a statistical analysis of bronchitis among 60,000 London Transport employees between 1952 and 1956. It is restricted to absences of 4 to 182 days, and compares the sickness rates among 5 different occupation groups of males and between those working in different geographical areas.

Bronchitis accounted roughly for 10% of the total sickness absence in this body of men. There was a close relation between the amount of bronchitis in any particular year and the occurrence of dense and prolonged fog. As a whole, country bus and coach staff had a better record than those working in central areas. Moreover those in the north-eastern section of London suffered more heavily than those in the south-western sector, supporting the hypothesis that atmospheric pollution is an important aetiological factor in this disease and repeating the findings of REID among London postman [this *Bulletin*, 1957, v. 32, 112].

Differences in the incidence of bronchitis in the 5 occupational groups studied suggest that only in conductors, who are thrown into close contact with the infections of passengers, is there an occupational factor of any aetiological significance. *T. O. Garland*

FUCHS, E. & GRONEMEYER, W. Zur Frage der Entschädigung beim Asthma bronchiale, insbesondere beim Gewerbeasthma. [**The Question of Compensation for Patients with Bronchial Asthma, especially Occupational Asthma**] *Deut. med. Woch.* 1961, Feb. 17, v. 86, No. 7, 298–302. [35 refs.]

This is a long and careful discussion of the existing legislation on compensation for disease in the German Federal Republic with special reference to bronchial asthma. This legislation which is quoted is insufficiently specific as regards bronchial asthma although its admission to compensation is not altogether excluded. Changes in this legislation are projected but there are many difficulties in the formulation of these changes. These difficulties which are here discussed at length with examples and references to the literature lie largely in the diagnosis of asthma and assessing its relation to occupation. *M. E. Delafield*

PELLETIER, M. Relations entre la profession et le nombre des anomalies pulmonaires et notamment tuberculeuses dépistées systématiquement dans le département de la Seine. [**Occupation and Pulmonary Disease, especially Tuberculosis. A Survey in the Department of the Seine**] *Arch. Malad. Professionnelles.* Paris. 1960, Dec., v. 21, No. 12, 727–34. [29 refs.]

The data analysed in this paper were obtained from records of mass radiography surveys carried out in urban communities in the Department of the Seine. France. The total numbers of examinations were 95,246 in 1956–57, 101,801 in 1957–58 and 103,295 in 1958–59. The incidences of pulmonary abnormalities and tuberculosis were found for each of 10 occupational groups.

Metal workers were responsible for the highest percentage of abnormalities during the 3 consecutive years (23·5 to 29). The figures for the other groups were: book-binding and printing 24·6 to 26·9, chemical works 10·7 to 17·6, clerical and administration 8 to 12·3, food and restaurants (including manufacture and sale of alcohol) 6·3 to 10·3, building 1·5 to 5·3, textiles 0·5 to 3·2, wood 0·6 to 2·3 and skins and hides nil to 1·1. The author notes that these figures have little intrinsic value because of the differences in the number of workers in the various groups.

The percentage incidence of pulmonary abnormalities and of tuberculosis (average for 1958–59) in the various groups was:

Abnormalities	%	Tuberculosis	%
1. Building	4·5	1. Food and Restaurant	0·24
2. Food	3·07	2. Metals	0·16
3. Books	2·62	3/4. Books, Printing and Chemicals	0·12
4. Chemicals	2·05	5. Building	0·08
5. Clerical	1·88	6. Clerical	0·07
6. Metals	1·74	7/8. Wood, Textiles	0·06
7. Textiles	1·29	9. Hides, not analysed	
8/9. Wood and Hides not analysed (too few workers)			

Although building workers provided the largest incidence of pulmonary abnormalities their incidence of tuberculosis was only 5th; metal workers were responsible for the highest percentage of abnormalities and had the 2nd highest incidence of tuberculosis.

It appears to be more profitable to carry out radiography surveys in small than in large establishments; there is closer contact in small establishments and hygienic conditions are more often absent.

The possible role of chemical irritants in rendering the upper respiratory tract more susceptible to invasion by pathogenic bacteria is mentioned. This could be partly responsible for the unfavourable findings in chemical workers.

The least unfavourable occupations appeared to be the wood and textile industries followed by clerical and administrative work. The incidence of tuberculosis was highest in workers in food industries (restaurants, sugar, oil and chocolate works, breweries and distilleries). Indulgence in alcohol may play a part in the high incidence of tuberculosis in food, building and metal workers. *H. G. Calwell*

STÖKLY, A. Gesundheitsgefahren beim Schweissen. **[Risks to Health in Welding]** *Ztschr. f. Präventivmed.* Zurich. 1960, Nov.–Dec., v. 5, Nos. 11/12, 329–42. [67 refs.]

This is a very comprehensive review and discussion of the actual and possible dangers to health occurring in welding. The first group of risks are those from materials and factors arising at the source of energy. Dangers may come from gases, namely, oxygen, ozone, nitrous gases, acetylene and carbon monoxide, or from ultraviolet light and electric shock. The only risk with oxygen is of fire from a spark when clothing of the welder becomes saturated with oxygen. Ozone may reach a dangerous concentration in gas shielded welding, causing, in a few cases, irritation of mucous membranes. Nitrous gases except in narrow places never cause any harm; they react with the iron cloud. At one time acetylene by its impurities such as phosphoretted hydrogen may have given rise to gastro-intestinal troubles: it is now supplied at the flame in a much purified condition. Carbon monoxide may be a risk in gas-shielded welding and the author recommends the exhaustion of gas near the welding point. Welders know about the danger of ultraviolet light and make use of the protection provided. There is more risk to third parties.

The second group concerns the material worked with, the metals or alloys and their coatings, as well as the electrodes and their covering, and the gases arising may come from either source. A large number of materials are mentioned as possible sources of trouble in the welding smoke. Iron may be a cause of siderosis of the lung from inhalation: the frequency of gastro-intestinal troubles, from ingested iron, is reported by several writers including DOIG and DUGUID [this *Bulletin*, 1952, v. 27, 165]. Where zinc or copper is welded, cases of metal fume fever may occur. Lead paint may be a source of lead poisoning. In the atomic industry there is a possible beryllium risk. Other possible sources of irritating vapours are calcium oxide, boron compounds, etc. Some materials are considered harmless; silica and asbestos in the electrode coverings, fluorine and manganese in the electrode are innocuous so far. Various metals such as aluminium, nickel molybdenum and others are acquitted.

[A summary of the paper is given but this should be taken as part of the text since it mentions matters not already discussed.] *Charles L. Sutherland*

KEEL, C. G. Unfallgefährdung und Unfallverhütung bei der Anwendung der modernen Schweissverfahren. **[The Danger and Prevention of Accident in the Use of the Modern Welding Process]** *Ztschr. f. Präventivmed.* Zurich. 1960, Nov.–Dec., v. 5, Nos. 11/12, 342–55, 4 figs.

The author is the Director of the Swiss Union for Welding Technique which has concerned itself since 1946 with all welding processes. He has thus access to sources of information regarding electric welding. As regards gas welding, the Regulation on Acetylene, Oxygen and Calcium Carbide, of 28th February, 1950, provides an experience of 10 years. It is claimed that Switzerland is the only place where hazards in electric welding have been reported regularly for 10 years. A table is given of the accidents each year in electric welding, in all there were 39 injured and 3 deaths. During this time the plants have increased from 8,000 to 15,000. With gas welding most accidents involve burners or pipes. Backfires in the pipes and breaking away of the pipes from the spouts are very common. An attempt is made to work out the accidents per year for the welding population but it is not entirely convincing. The prevention of accidents is given in detail.

[Most of these accidents are covered in the publication of the British Factory Department. *Memorandum on Safety Measures required in the Use of Acetylene Gas and in Oxy-acetylene Processes in Factories* (Form 1704), and the *Memorandum on Electric Arc Welding*.] In addition to warning against the use of copper in appliances with acetylene, the author does not recommend the use of steel of any kind, including rust-free chrome nickel steel, in connexion with oxygen.

The Union for Welding Technique is carrying out investigations into such matters as the production of copper acetylide, the cause of blowbacks, and the safe pressure of acetylene containers.

Charles L. Sutherland

OCCUPATIONAL DISEASES

SOUTH AFRICAN COUNCIL FOR SCI. & INDUST. RES. **Proceedings of the Pneumoconiosis Conference held at the University of Witwatersrand, Johannesburg, 9th–24th February, 1959** [ORENSTEIN, A. J. (Edited by)]. pp. xvi + 632, numerous illustrations. [Numerous refs.] 1960. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [£6.]

[During the past 30 years, 4 conferences of international experts have been held to review current knowledge of and research into the dust diseases of the lungs. The first was held at Johannesburg in 1930 (this *Bulletin*, 1931, v. 6, 513) under the aegis of the International Labour Office, which subsequently organized similar meetings at Geneva in 1938 (*ibid.*, 1940, v. 15, 459) and at Sydney in 1950 (*ibid.*, 1954, v. 29, 626). In 1930 the study of the dust diseases of the lungs was almost entirely concentrated on silicosis due largely to the problems created by the disease among gold-miners on the Witwatersrand. Thereafter attention extended

to mineral dusts other than free silica until ultimately in the early 1940s the field was dominated by coal dust and pneumoconiosis of coal-workers particularly in South Wales. Unfortunately, even at meetings of international experts, speakers do not always distinguish precisely between the different varieties of pneumoconiosis and confusion arises from pronouncements influenced by individual experience in a particular field of mining or industry or in research related thereto.

At the request of the South African Government the South African Council for Scientific and Industrial Research convened a conference on pneumoconiosis at the University of Witwatersrand, Johannesburg, from 9 to 24 February, 1959. Professor S. F. Oosthuizen, Pretoria, was appointed President and Dr. A. J. Orenstein, Director of the South African Pneumoconiosis Research Unit, acted as Secretary-General. 67 invited members participated, 35 medical and 32 non-medical, of whom 17 were from Belgium, Germany, Italy, Switzerland, Great Britain and United States of America. The non-medical members included mining engineers, physicists, chemists, serologists, physiologists and statisticians. In addition a number of observers from various countries attended. Dr. A. J. Orenstein and Dr. W. E. George, New South Wales, Australia, an observer, were the only persons present who had attended the first conference in 1930.

Readers of the Proceedings should understand clearly the terms of reference and purpose of the conference as otherwise they might criticize the omission of certain topics. Essentially the members were concerned almost exclusively with the scientific aspects of pneumoconiosis. The medico-legal aspects, workmen's compensation, were excluded from the programme. The principal purpose of the Conference was stated thus: "To review recently acquired and not generally known knowledge in all the scientific disciplines concerned with the study of the aetiology, pathology, and prevention of pneumoconiosis, and to make recommendations on further research which would most likely be rewarding."

80 papers were presented and discussed and finally a series of recommendations were adopted by the Conference. The present Proceedings comprise the text of the papers and a record of the discussions. Finally the recommendations are set out. Many of the papers had already or have since been published in scientific journals and reports throughout the world. The merit, however, of this volume is that papers on the same and cognate subjects, representing research and experience in many countries, are conjoined and discussed as a group.]

Dr. Orenstein, the editor, has very commendably arranged the papers not only in groups covering allied topics but so that they present a continuous and developing account of the subject. Thus the opening papers deal with the physical and chemical characteristics of various dusts, their production in mining and other operations, methods of sampling and measurement. *What Should be Measured in Dust Sampling?* (pp. 8–11) by Dr. A. J. Orenstein reflects his long intimate experience among gold-miners and contains much practical good sense and wisdom. In *Source of Dust in Mines and Methods of Prevention at the Source* (pp. 39–42) J. de V. Lambrechts (South Africa) rightly emphasized that "the primary policy is the prevention of dust at its source." In the discussion W. H. Walton (Great Britain) commented that this fact and others should be taken into account at the design stage of machines; "In fact they rarely are. The tendency of mechanical engineers is to improve efficiency, reduce weight and increase output." Professor T. F. Hatch (U.S.A.) made this cogent contribution to the discussion on sampling. "Through the use of the physical instrument we should be trying to predict what would happen to a man if he were there in place of the instrument. We are sometimes inclined to forget this and get so enamoured of our beautiful physical devices that the point is overlooked that this is just a substitute for man. The design of the instrument and the evaluation of its operating characteristics should be based more on the understanding of how man acts in the dusty atmosphere than on physics alone."

E. J. King and G. Nagelschmidt (both Great Britain) reviewed their wide experience of *The Physical and Chemical Properties of Silica, Silicates and Modified Forms of these in Relation to Pathogenic Effects* (pp. 78–83). From numerous previous contributions this work is already well known and highly regarded throughout the world. *The Bio-Assay of Dust with particular Reference to Experimental Methods* (pp. 84–92) by Professor A. J. Vorwald (U.S.A.) contains a notable apologetic of the experimental method in laboratory animals. The paper by Professor T. F. Hatch on *Respiratory Dust Retention and Elimination* (pp. 113–130) gives an impressive picture of the great ingenuity of the experimental physicists in the design and completion of complex experiments to simulate conditions in the lungs. It emerges that knowledge in these fundamental aspects of pneumoconiosis is very imperfect and is "a major area which requires further research". That there are still important areas of controversy among experts on pneumoconiosis was clearly revealed in the discussion on Professor A. J. Vorwald's contribution on *Inhaled Submicroscopic Particles in the Pathogenesis and Pathology of Silicosis* (pp. 137–142) [sub-microscopic was defined as particles smaller than 0·1 micron]. Dr. Nagelschmidt said, "I do not believe that the small particles are very important. . . . Unless I am given very convincing proof, I shall continue to believe that the most dangerous size range is 1–2 microns". The editor inserts this note: "The discussion revealed that it is important to ascertain the relation of particle size to the pathogenicity of dust and that there is at present no clear information on this".

At the original 1930 Conference Strachan and Simson described the pathology of gold-miners' silicosis in South Africa. In the interval preventive measures have altered the picture as shown by Dr. Ian Webster (South Africa) in a paper entitled *Some Aspects of Pathology of Silicosis found in Miners from the South African Gold Mines* (pp. 156–169). This was followed by an interesting and informative series of papers and discussions on the problems of emphysema (bullous, focal and centrilobular) and bronchitis in relation to various types of pneumoconiosis. Members

attested to the great value of Gough-Wentworth macro-sections in this field of study. Professor J. GOUGH (Great Britain) at the conclusion of his contribution on *Emphysema in Relation to Pneumoconiosis* (pp. 200–204) expressed this opinion: "When, however, there is a combination of focal emphysema due to dust and centrilobular emphysema it would seem reasonable to regard both as contributing to physical disability, and to death if that is due to cor pulmonale or respiratory failure."

From consideration of the associated pulmonary conditions there followed naturally a series of papers on cardiac complications, particularly cor pulmonale. Professor F. LAVENNE (Belgium) (pp. 216–219) gave a comprehensive account of the researches into cor pulmonale and the pulmonary circulation which he and his colleagues had made at the Institut d'Hygiène des Mines, Hasselt, Belgium.

On the subject of radiological diagnosis of pneumoconiosis Dr. E. SAMUEL (South Africa) discussed the important issues involved in *How Much Physiological Information can be obtained from a Plain Radiograph?* (pp. 263–266). Cognate to this 3 highly interesting papers followed on the effects of ageing: *Changes in Clinical, Pathological and Radiological Findings due to Ageing* (pp. 275–276) (J. GOUGH); *Radiological Manifestations of Pulmonary Changes due to Ageing* (pp. 277–279) (E. SAMUEL); and *Changes in Lung Function with Age* (pp. 279–285) (J. C. GILSON, Great Britain). There is a touch of the macabre in the "hanging" technique described by Dr. E. P. PENDERGRASS (U.S.A.) for the post-mortem radiography of the lungs.

HOUBERECHTS (pp. 299–300) (not "Houbrechts") and NAGELSCHMIDT (pp. 290–298) discussed the role of free silica in the pathogenesis of coal-workers' pneumoconiosis based on their respective experience in Belgium and Great Britain. This was followed by KING (pp. 301–321) and GOUGH (pp. 322–324) who spoke on infective pneumoconiosis from the viewpoints of the experimentalist and the pathologist. Dr. J. ROGAN (pp. 338–347) described the Pneumoconiosis Field Research project of the National Coal Board in Great Britain, and Dr. J. C. GILSON followed with an outstanding review of the *Epidemiological Methods Developed for the Study of Coalworkers' Pneumoconiosis and their possible Relevance to the Study of Silicosis* (pp. 348–356).

At international conferences members are alert for the announcement of a new discovery. On this occasion this came in Dr. J. C. WAGNER'S (South Africa) communication on the *Pathological Aspects of Asbestosis in South Africa* (pp. 373–381) in which he described his studies of mesothelioma of the pleura. E. C. VIGLIANI and B. PERNIS (Italy) (pp. 395–407) and I. WEBSTER, H. PALMHERT, D. R. COOPER, R. E. SILVERTON, C. S. ANDERSON, A. ZOUTENDYK and G. MCNAB (pp. 408–413) comprehensively reviewed their studies on *The Immunological Approach to Silicosis.* Several speakers followed with papers on the chemical (including enzymes) changes induced by fibrogenic and inert dusts. Dr. L. D. ERASMUS (South Africa) from a study of *Scleroderma in Gold Mines* (pp. 426–435) concluded that "There is evidence which strongly suggests that there is a high incidence of scleroderma in gold miners as compared with non-miners". On the subject of the *Assessment of Pulmonary Disability* (pp. 511–515), Professor P. H. ROSSIER (Switzerland) was, as always, provocatively stimulating by his heterodoxy or perhaps non-conformity.

Following a series of contributions on pulmonary disability recording experience in different countries there was *A Panel Discussion on Pulmonary Function Testing* (pp. 534–538) under the leadership of Dr. B VAN LINGEN (South Africa).

The concluding papers covered a wide variety of topics including exercise tolerance, plethysmography and somatotyping and clinical problems of separate pneumoconioses and their complications. In the final chapter a summary of the answers is given to 14 specific questions posed by the Dust/Engineering Group.

The Recommendations Adopted by the Pneumoconiosis Conference make a formidable list by any measure. They are arranged in 3 groups.

I. In the field of aetiology and pathology (19 recommendations).

II. In the field of physiology, radiology and clinical medicine (6 recommendations).

III. In the field of dust and engineering (25 recommendations).

[This volume is an indispensable work of reference for all throughout the world who are interested in the pneumoconioses. The text is not without errors but these are relatively few having regard to the length of the book. Readers will find some of the discussions confusing and in fact misleading. On the whole the Conference achieved its objects and in conjunction with the Proceedings will endure as a tribute to the dedicated lifework of Dr. Orenstein. In summing up it may not be inappropriate to adapt the words of Cecil Rhodes: so little known, so much to know. It is, however, heartening to see that the engineers have accepted the challenge presented by dust and are advancing to leadership.] *A. Meiklejohn*

MILLER, S. E. **New Concepts of Industrial Dust Diseases.** *Indust. Med. & Surgery.* Miami. 1961, Jan., v. 30, No. 1, 16–19. [18 refs.]

A classification of the pneumoconioses based on pathological effects is presented, grouping them into major, minor and benign pneumoconioses. The major type includes classical silicosis, Shaver's disease, asbestosis and coal-miners' pneumoconiosis. The minor type includes diatomaceous earth pneumoconiosis from amorphous silica, and the silicatosis from pure micas, clays and felspars, as well as conditions arising from vegetable dusts, such as byssinosis, bagassosis and weavers' cough. The benign pneumoconioses include siderosis, stannosis, etc.

In the United Kingdom the pneumoconioses are by definition, legally at any rate, fibrotic conditions of the lung and therefore do not include byssinosis and possibly the effects of other vegetable dusts.

In describing the production of the classical silicotic nodules, the author quotes the experimental evidence

of Gross *et al.* [this *Bulletin*, 1959, v. 34, 347], as showing that most silicotic nodules originate in or on the alveolar walls and that the collagenous fibres spring from the cells of the alveolar walls.

Charles L. Sutherland

Chatgidakis, C. B. **A Study of the Bronchial Mucous Glands in White South African Gold Miners. A Histological Survey.** *Arch. Environment. Health.* Chicago. 1960, Oct., v. 1, No. 4, 335–42, 6 figs. [16 refs.]

[For the purpose of workmen's compensation there has been a progressive extension of the connotation of pneumoconiosis resulting in a more liberal interpretation in favour of the workman. The diagnosis of pneumoconiosis in the individual case, however, involves the identification of certain radiographic changes in the lungs. Workmen—in Great Britain particularly coal-miners—in dusty occupations not infrequently suffer from severe pulmonary disability—generally certified as chronic bronchitis—but in the absence of the necessary radiographic changes they are excluded from compensation benefits under the Pneumoconiosis Schemes. Throughout the world this situation in recent years has increasingly raised the question: "Should the bronchitis of miners be regarded as occupationally induced or not?".]

Towards the elucidation of this issue Dr. C. B. Chatgidakis, wife of Dr. B. J. P. Becker [Professor of Morbid Anatomy and Histopathology, University of Witwatersrand], pathologist, South African Pneumoconiosis Research Unit, has made intensive researches into the bronchi in health and disease. The present paper is only part of this work [for more detailed reports including other contributors see Proceedings of the Pneumoconiosis Conference, Johannesburg, 1959, p. 523]. From a histological survey of the bronchial mucous glands in white gold-miners and a control group of white non-miners, both male and female, the following conclusions emerged:

"It was shown that enlarged bronchial mucous glands with excessive mucous secretion and dilated ducts is much commoner in males and apparently age in itself does not appear to affect them.

"The results suggest that enlarged bronchial glands with excessive mucous secretion and dilated ducts occurred with increased frequency as the silicosis became more severe. But this is found with great frequency in elderly male non-miners and the miner with silicosis is an ageing male who is subject to all the usual non-industrial bronchial diseases. In addition, he is a heavy smoker.

"The bronchi of fifteen non-smoking gold miners, with varying degrees of silicosis, were examined and it is suggestive that silicosis in itself plays no part in the enlargement of these glands.

"There appears to be no increased incidence of enlarged mucous glands in the bronchi of cases of acute pneumonia and tuberculosis.

"No significant histochemical differences have been observed in the bronchial gland mucus of miners and non-miners."

A. Meiklejohn

Dofny, E. Evolution de l'image pneumoconiotique après cessation de l'exposition aux poussières. [**Progression of Radiographic Findings in Pneumoconiosis after Exposure to Dust has Ceased**] *Rev. Inst. Hyg. des Mines.* Hasselt. 1960, v. 15, No. 3, 79–83.

In this study the X-ray findings in 144 miners at the time they ceased to be exposed to dust were compared with the radiographic appearances 3 to 10 years later. The classification of the Belgian Institut d'Hygiène des Mines was used and the author found that progression had occurred at all stages of pneumoconiosis. Thus 36% of the miners with doubtful lesions (Group 1), 63·5% of those with lesions in the initial stage (Group 2), 92·16% of those with numerous small opacities (Group 3) and 100% of those with massive shadows (Group 4) showed progression. In Group 1, which comprises films in which the lung fields are either regarded as clear or show "reticulation", there were 25 cases. Of these, 9 were originally considered clear and only 2 had progressed, but of the 16 classified as showing "reticulation" progression had taken place in 7 cases. One of the latter sub-group showed coalescence but the remaining 8 had progressed only to a small extent. Among 24 cases held to be of Group 2, 14 had progressed: in one coalescence had developed but the others had evidence of only a slight degree of progression. There were 51 cases in Group 3 and only 4 showed no change: in 21 cases coalescence had developed and in 2 cases progressive massive fibrosis had occurred while in the remaining 24 only a slight increase of nodulation was present. Group 4 comprised 35 cases and 23 had progressed from coalescence to gross massive fibrosis. The first two groups never reached the stage of coalescence but in Groups 3 and 4 progression is the rule and in the latter 64% of cases showed deterioration. It was noted that the pinhead variety of pneumoconiosis had little tendency to progress.

The fact that this study was based on only 144 cases is emphasized and the warning is given that definite conclusions cannot be drawn from so small a number.

G. F. Keatinge

Brun, J. & Pozzeto, H. Une complication méconnue de la silicose. Les ruptures ganglionnaires endobronchiques. [**A Little Recognized Complication of Silicosis. Rupture of Lymphatic Glands into Bronchi**] *Arch. Malad. Professionnelles.* Paris. 1960, Oct.–Nov., v. 21, Nos. 10/11, 622–34.

Enlargement of mediastinal lymphatic glands, particularly the hilar group, is a well-recognized feature of silicosis. Many authors have described the various pathological and radiological changes which occur in these glands and the effects which they may cause in adjoining structures such as the bronchi and oesophagus. By contrast there are few references to cases in which caseation or necrosis of a gland has resulted in a fistulous opening into a bronchus.

This paper describes this condition and its identification clinically, radiologically and by bronchoscopy. Stress is placed on the importance of diagnosing such

an occurrence in relation to the progress and prognosis in individual cases of silicosis.

[Readers who are particularly interested in this aspect of pneumoconiosis are referred to the following comprehensive study; H. POZZETTO: *Anthracosilicose ganglionnaire et ruptures endobronchiques* (Thesis, p. 96, Lyons, 1960).] *A. Meiklejohn*

LEAL Y LEAL, J. Reparación de la silicosis (legal, médica y social). [**Rehabilitation in Silicosis (Legal, Medical and Social)**] *Med. y Seguridad del Trabajo.* Madrid, 1960, Apr.–June, v. 8, No. 30, 57–73.

Silicosis was officially recognized in Spain as an occupational disease in 1936 and the problems which have arisen and the administrative methods which have been developed in dealing with it since that time are critically reviewed. Proposals are put forward for an improved system and a formal scheme for assessing the degree of disablement due to pneumoconiosis is suggested. Prognosis and difficulties in resettlement are dealt with in detail: it is held that while the tuberculous patient requires graded work, in the case of pneumoconiosis it is retraining which is always the need.

Reference is made to the experience of resettlement gained in other countries and special admiring mention is made of the pioneer work at Papworth Village Settlement.

Although the author realizes that the problem is not wholly a medical one, he feels that medical and technical methods for the control of silicosis have not been pursued in Spain with as much vigour as in some other countries. *G. F. Keatinge*

GUTIÉRREZ DEL OLMO, J. Prevención, médica de la silicosis. [**Medical Prevention of Silicosis**] *Med. y Seguridad del Trabajo.* Madrid. 1960, Apr.–June, v. 8, No. 30, 74–86, 2 figs.

This paper was presented at a colloquium which was held in Madrid during April 1960 under the auspices of various governmental and other bodies concerned with occupational health and safety in Spain. Relevant paragraphs are quoted of the Decree which in 1947 brought into being the organization for the care of occupational disease in that country. The arrangements made to implement the requirements of this decree, which include X-ray of chest at entry and periodic follow-up of all workmen engaged in certain scheduled occupations, are described.

In these surveys which have averaged about 50,000 examinations annually between 1955 and 1958, the incidence of silicosis has ranged from 1·90% in the pottery industry to 8·19% among gold-miners. Pneumoconiosis is considered separately and had its lowest incidence among cement workers at 0·2% and its greatest in fluorspar miners at 9·37%. The author recommended that bronchitis and emphysema should be included in the schedule of occupational diseases: they can be a cause of serious disablement in any dusty trade but are more severe in atmospheres heavily charged with dust of vegetable origin. *G. F. Keatinge*

CARTOUZOU, G. & DUPLAY, J. Données chimiques sur le granulome silicotique péritonéal expérimental du cobaye et du rat. [**Chemical Observations on Peritoneal Silicotic Nodules induced Experimentally in the Guineapig and the Rat**] *C.R. Soc. Biol.* 1960, v. 154, No. 7, 1459–62.

This paper and the one following were read at the Biological Society of Marseilles on 24 June, 1960. The work was carried out in the Faculty of Medicine and Pharmacy at Marseilles. The chemical analyses were based on material (silicotic nodules) obtained from 2 separate experiments.

In experiment I, 60 guineapigs and 15 rats were injected (4 gm./kgm.) intraperitoneally with silica particles of 20 μ diameter. The resultant silicotic nodules were excised at the end of 2 months. Experiment II comprised 15 guineapigs and 30 rats which were injected (0·5 gm./kgm.) intraperitoneally with silica particles under 3 μ diameter and the nodules were excized after 1 month.

The 2 species of animal reacted differently to the injected silica. Thus 20 μ silica produced lesions which were 3 times richer in collagen in the rat than in the guineapig. 3 μ silica was considerably more fibrogenic than 20 μ silica in the guineapig. Among the items investigated were weight of lesions, water and silica content of nodules, percentage amount of silica recoverable from peritoneum, and content of nitrogen, protein, hexosamines and hydroxyproline—the amino-acid characteristic of collagen. The collagen and elastin fractions of proteins were also determined. Details of the results are summarized in 2 tables. *A. Meiklejohn*

CARTOUZOU, G., LISSITZKY, S., DEPIEDS, R. & DUPLAY, J. Étude chimique des constituants protéiques du granulome silicotique péritonéal expérimental du cobaye et du rat. [**Chemical Study of the Protein Constituents of Peritoneal Silicotic Nodules induced experimentally in the Guineapig and the Rat**] *C.R. Soc. Biol.* 1960, v. 154, No. 7, 1463–8.

This study is an extension of the preceding one [see above]. The chemical methods employed are described and the results tabulated. It was observed that non-collagen proteins accounted for 60–70% of total protein content of nodules. Soluble collagen occurred only in small amount and of this the acid-soluble fraction was 3 to 4 times greater than the alkaline-soluble fraction. *A. Meiklejohn*

FRIEDBERG, K. D. Quantitative Untersuchungen über die Staubelimination in der Lunge und ihre Beeinflussbarkeit im Tierexperiment. [**Quantitative Animal Experiments on Dust Elimination from the Lungs and on Ways in which it can be Modified**] *Beiträge z. Silikose-Forschung.* 1960, No. 69, 1–99, 21 figs. [Numerous refs.]

This is an important paper in which the author reviews the results of five years' work. In the course of it about 5,000 rat lungs have been analysed for silica.

When dust is inhaled, those particles which are deposited on the ciliated epithelium are removed in the course of a few hours. This first rapid phase of elimination is not considered in the present work. Particles which are deposited beyond the terminal bronchioles can be dissolved, stay in the lung, be removed to the lymph glands or they can again, more slowly, reach the ciliated epithelium and be removed along the escalator. By lung dust analysis it is possible to study this slow phase of dust elimination [plus losses due to dissolution].

The author used a dusting technique developed by POLLEY of Göttingen which is described briefly. Dust is produced by grinding 4 $cm.^2$ prisms of sandstone with a rotating carborundum wheel, the dust concentration being controlled by the rate of advance of the prism. The dust, diluted with air, is led into a tunnel in which up to 40 rats in single cages can be exposed for several hours. An earlier box-shaped installation with a capacity of 24 rats is also described. A fairly constant dust cloud is produced which is controlled by tyndalloscope. Most experiments were made with a cloud which contained 45,000 particles per cc. of unspecified size range. Membrane filter measurements showed this cloud to contain, on an average, 180 $mgm./m.^3$ of dust and a size analysis obtained by electron microscopy gave a distribution of particle numbers as 33% below 0·2 micron, 78% below 0·5 micron and 99% below 5 micron. The sandstone, and the airborne dust, contained 85 to 95% of quartz according to petrographic and X-ray analysis.

Methods of killing the rats, removing the lungs and analysing them for silica by the molybdenum blue technique after fusion of the lung ash are described in detail. Duplicate analyses on batches of 5 to 20 animals for each treatment were carried out and the results were assessed statistically. All lungs were freed from blood before their removal from the chest, and controls contained 10 μgm. or less of SiO_2. In the course of the work 6 different strains of rats were used.

The first group of experiments (with over 300 analyses for SiO_2) concerns the elimination of between 0·2 and 0·8 mgm. of SiO_2 per lung in the course of 30 days. The elimination rate was constant and of the order of 65% of the amount found one day after the dust exposure. The results are given in great detail in form of tables and illustrations. They were all obtained with one particular strain of rats.

In the next group of experiments 4 other strains of rats were used and in 2 experiments the age of the rats was varied. Rat weights at 2 months were about 200 gm. and at 5 months about 270 gm. In some of the experiments the time was increased from 30 to 90 days. There was no effect due to age but one strain (described as *Winkelmann Ratten*) showed a significantly lower rate of elimination so that after 3 months 20% of the initial dose was still present as against 10% for Sprague Dawley rats. Calculated half-lives of the dust for these strains were 37 and 20 days respectively.

When higher dust doses were given—1·5 mgm. in 3 daily 5-hour exposures and 3 mgm. in 5 daily 10-hour exposures—elimination, followed for 1 month, and for 1, 3 and 6 months respectively, was significantly reduced and the calculated half-life for the 3 mgm. dose rose to 93 days. The author explains this effect by assuming that there was a shortage of phagocytic cells from the alveolar epithelium and that consequently the dust could penetrate into the interstitial tissue from which removal was slowed down. In these experiments it was also possible for the first time to demonstrate rather variable amounts of silica in the lymph glands.

The initial dose had always been determined 16 to 24 hours after the end of the dust exposure and in a separate series it is shown that the differences in dust uptake found between rats killed immediately and 24 hours after the end of dust exposure did not reach significance levels.

Separate analyses of the 3 right lobes and ventral and dorsal portion of the left lobe showed small differences when the results were expressed as percentage of dried weight. The highest values for dust uptake were found in the right upper and ventral left lobes. Elimination rates were rather similar for all parts of the lung, in contrast to the results of STOKINGER *et al.* [this *Bulletin*, 1952, v. 27, 341] with uranium oxides. In a final review of this first part of the paper the author points out differences between his own results and those of other workers and stresses that the higher elimination rates found by him are probably the result of more "physiological" conditions, *i.e.* lower dust concentrations. He does not believe that solubility of his quartz dust could be a factor.

The second part of the paper deals with attempts to modify the elimination rate by various treatments. Each attempt had its own controls and the first part was a review of all the controls. Most results were obtained by comparing the silica content one day and 30 days after the end of the dust exposure. When the rats were kept warm, at 32° C., which seems to be the maximum which they tolerated, there was no clear difference from normal although a few rats had only taken up surprisingly little dust. When the rats were kept cold, at 6° C. and 4° C., dust elimination was significantly reduced. Retention was 44 and 50% as against 30% for the controls. Other treatments which reduced elimination were: subcutaneous injection or inhalation of Evans Blue, which in some experiments doubled the amounts retained after 30 days, injection (?) of a soluble dextran (Macrodex), and previous dusting with graphite which in one experiment completely blocked elimination of silica, in another reduced it by half and in 2 further experiments was ineffective.

Most treatments were without effect on the elimination rate. In this class there was exercise after the dust uptake (swimming or running), chlorpromazine as a sedative, GEIGY'S Micoren and Pervitin as stimulants, ammonium chloride and acetazolamide as acidosis-producing agents, polyvinyl pyrrolidine and various steroids, and inhalation of salt or aludrin aerosols. The latter 2 reduced elimination by a few per cent. but although statistically significant the effect was very small indeed. A similarly small significant increase in elimination was seen after 2 or 3 intraperitoneal injections of homogenized chick albumin.

The author comments that this work is only a beginning but that it has shown that it is possible both to increase or to reduce experimentally the elimination of inhaled dust. *G. Nagelschmidt*

JORDAN, J. W. **Pulmonary Fibrosis in a Worker using an Aluminium Powder.** *Brit. J. Indust. Med.* 1961, Jan., v. 18, No. 1, 21–2, 2 figs. [12 refs.]

A female aged 26 complained of increasing dyspnoea, accompanied by slight cough and sputum, pleuritic chest pain, loss of appetite, weakness and sweating. For 5 years she had been employed filling fireworks by hand with a mixture of aluminium powder and potassium perchlorate. She worked alone in a small room which was not usually dusty, but there was much spillage, and high concentrations of airborne dust occurred after sweeping which was carried out several times daily. Examination showed slight clubbing of fingers and toes, displacement of trachea to right, poor chest expansion and the presence of moist sounds on auscultation. The radiograph confirmed the tracheal displacement and showed fine granular shadowing throughout both lung fields, diaphragmatic adhesions and upward displacement of the hila. There appeared to be a pulmonary cyst and a small effusion at the extreme right apex. 5 months later there was a small pneumothorax there which slowly disappeared with rest in bed. A guineapig into which a specimen of the patient's sputum had been injected developed a tuberculous lesion, but this was the only one of many samples over a 5-year period, which gave a positive result for tubercle bacilli. 4 years after the initial examination the patient developed pains in the larger joints and fusiform swellings of the fingers. The latex screen test and the Rose Waaler reaction were positive and subsequently the rheumatoid arthritis became more marked.

It is stated that the particle size of the aluminium powder varied and that many particles were less than 5μ but no results of counts or analyses are given. Lung biopsy was considered but for good reasons, including the possible danger to the patient particularly in view of the pneumothorax, was not carried out. [The aetiology of this case must be regarded as doubtful: the author's contention that the condition is the result of the inhalation of aluminium must obviously be given careful consideration, but as he himself admits, proof is at present lacking.] *A. T. Doig*

MITCHELL, J., MANNING, G. B., MOLYNEUX, M. & LANE, R. E. **[Pulmonary Fibrosis in Workers exposed to Finely Powdered Aluminium]** *Brit. J. Indust. Med.* 1961, Jan., v. 18, No. 1, 10–20, 15 figs. [15 refs.]

The authors describe the clinical, radiological and pathological features of pulmonary fibrosis in aluminium workers, basing their observations on 6 cases found in 27 workers examined out of 30 known to have been at risk. 2 of the cases terminated fatally, one of them having previously been fully described by MITCHELL [this *Bulletin*, 1959, v. 34, 906] who also mentioned the occurrence of the second in a footnote to his paper. All the workers were employed in a small factory which produced aluminium powder in two grades by a stamping process. A coarse powder used for paint contained much stearin but in the manufacture of the fine "pyro" powder, used for fireworks, the amount of stearin used was kept as low as possible and in 1952 it was largely replaced by mineral oil. The distribution of the cases showed that "pyro" powder was the most harmful, the 2 men who died having worked solely with this, for only 2·7 and 3·5 years respectively. The workers were exposed to high concentrations intermittently during charging and emptying the stamping machines and weighing and screening the powders; these fluctuated considerably but estimates in screening showed a mean of 95 mgm./cu.m. of respirable dust. 70% of the particles were 5μ or less in diameter and chemical analysis showed metallic aluminium 81·4%, aluminium oxides about 17%, stearin 0·5%, silicon 0·5%, with traces of other metals but no detectable beryllium. Increasing dyspnoea was the prominent symptom in the fatal cases, but 3 of the 4 who survived were symptomless or nearly so, the other suffering from fairly marked dyspnoea and tiredness. No patient showed finger clubbing. X-ray appearances varied from very slight opacities in one case to very severe abnormalities in the fatal cases. The pulmonary opacities tended to be more numerous in the upper zones, and the X-ray appearance in the developed case indicated very marked fibrosis particularly in the upper parts, the hilar regions and indeed the whole mediastinum being pulled upwards, resulting in kinking of the oesophagus and trachea, and raising of the diaphragm. Pneumothorax, a feature mentioned in the literature, was not present. On post-mortem examination the lungs were found to be intensely fibrotic, the fibrosis being generalized, diffuse and non-nodular and in one case largely acellular. There was no evidence of tuberculosis, sarcoidosis or other specific disease. Quantitative analyses showed the presence of aluminium.

Lung function tests carried out on the non-fatal cases showed no abnormality in the slightest case, and varying degrees of ventilatory defect due to fibrosis in the other 3. There was no important degree of airway obstruction or emphysema and diffusing capacity was reduced only in proportion to mechanical defect, thus differing somewhat from asbestosis.

The illustrations include well reproduced radiographs and two lung sections, and a good review of the literature is given. *A. T. Doig*

MCLAUGHLIN, A. I. G. & HARDING, H. E. **The Causes of Death in Iron and Steel Workers (Non-Foundry).** *Brit. J. Indust. Med.* 1961, Jan., v. 18, No. 1, 33–40, 7 figs. [15 refs.]

The clinical, occupational and pathological (post-mortem) findings in 10 grinders and 16 other non-foundry workers in iron and steel are reviewed. All the cases described had been reported to the coroner because of accident, suicide, sudden death or because a claim for compensation was contemplated by relatives. Thus they represent only a small proportion of the deaths which have occurred during the 15-year period of collection by the authors of pathological material to study the causes of death in iron and steel foundry workers [this *Bulletin*, 1950, v. 25, 1078; 1957, v. 32, 157].

In all of the 10 grinders silicosis or mixed dust fibrosis

or both were found mainly in a fairly advanced stage though the immediate cause of death varied from case to case. 3 had massive silicosis; 4 others had a mixture of moderate silicosis and mixed dust fibrosis; 1 had moderate silicosis, another moderate mixed dust fibrosis, and the 10th had slight mixed fibrosis and extensive tuberculosis which was the actual cause of death. Fibrosis due to dust was a definite factor in the cause of death in these cases: in 3 others it was doubtful and in 4 cases dust and fibrosis was not a factor. The average age at death of these 10 cases was 58·9 years.

13 different occupational categories were included among the remaining 16 cases and the risk of onset of pneumoconiosis among them was found to be small though not absent.

Details are given of the occupational and clinical histories and post-mortem findings including chemical analysis of the lungs in 12 cases.

The authors conclude that grinding is a less dangerous trade than it was 50 or 100 years ago, and grinders now live longer. The improvement in their health results from a combination of factors and among those affecting particular employment, the replacement of sandstone by artificial grindstone in many works, provision of exhaust ventilation and a general raising of the standard of housekeeping in works are mentioned. Nevertheless it is held that more remains to be done to improve the working conditions of grinders. *G. F. Keatinge*

SADOUL, P., GUILLERM, J., AUBERTIN, N. & GARBAGNI, R. Sulla pneumoconiosi dei minatori del ferro e sue conseguenze funzionali. [**Pneumoconiosis in Iron Miners and its Functional Consequences**] Reprinted from *Minerva Med.* 1958, Dec. 12, v. 49, No. 99, 4689–93, 3 figs. [12 refs.] English summary (9 lines).

The minerals which are extracted in the iron mines of Lorraine include calcium salts and iron oxide with a low proportion of silicates but seldom any free silica. Such inert dusts should lead to only a simple pneumoconiosis and to no specific pathological reactions.

The authors have investigated 320 cases of pneumoconiosis among iron miners of Lorraine, whose exposure to this dust had lasted 15–25 years. On the basis of the X-ray findings, and in accordance with the Cardiff-Douai classification, they have grouped the series under 5 type headings. Only 29 (9%) gave "massive" shadows; the other 91% showed a lighter degree of involvement, as represented by reticulation only, pin-heads (1 mm. in diameter or under) or micronodules (1–3 mm. diameter). In this paper the authors discuss the pathological anatomy of iron pneumoconiosis, when it is not complicated by silicosis, and its functional repercussions, and they conclude that the condition may be more serious than the measurements of lung volume and of respiratory ventilation suggest. The condition is not free from the risks of emphysematous or circulatory failure, as in silicosis, and the affected workman should receive adequate assistance to allow for the necessary rest. *J. Cauchi*

MED. D. LAVORO. 1960, Dec., v. 51, No. 12, 753–803, 27 figs. [Numerous refs.] Atti del simposio internazionale sulle malattie polmonari da polveri. Clinica del Lavoro di Milano, 12 giugno 1960. [**Symposium on Dust Diseases of the Lungs, Milan, June 1960**]

The paper by R. S. F. SCHILLING (*Recent Studies of Byssinosis in the Lancashire Cotton Industry*) is an account of work already reviewed in this *Bulletin* [1960, v. 35, 644]; and the same is true of the papers by A. BOUHUYS (*Experimental Studies on Byssinosis in Man*) [*ibid.*, 1960, v. 35, 758] and H. ANTWEILER (*The Liberation of Histamine by Extracts of Cotton Dust and its Relation to the Pathogenesis of Byssinosis* [in German]) [*ibid.*, 1961, v. 36, 238].

The final paper by B. PERNIS, E. C. VIGLIANI and G. CAVAGNA (*The Role of Endotoxins in the Pathogenesis of Dust Diseases in Textile Workers*) puts out a suggestion which is covered by their summary:—

"A variety of occupational diseases connected with the inhalation of vegetable dusts, especially in the textile industry, have certain symptoms in common such as fever, cough, dyspnea, general malaise; in most cases the symptoms are more prominent or appear only on Monday or on resuming work after one or more days of absence. The symptoms of these diseases and the Monday fever led to the hypothesis that they are due to the inhalation of the endotoxins of Gram-negative bacteria that contaminate the various vegetable materials, the Monday fever being connected with the phenomenon of tolerance to the endotoxins. Support for this view is given by demonstrating the constant presence of endotoxins in industrial cottons and by showing the similarity of the effects of the injection and of the inhalation of cotton extracts and of purified endotoxins in rabbits and in man." *Charles Wilcocks*

MAIR, A., SMITH, D. H., WILSON, W. A. & LOCKHART, W. **Dust Diseases in Dundee Textile Workers. An Investigation into Chronic Respiratory Disease in Jute and Flax Industries**] *Brit. J. Indust. Med.* 1960, Oct., v. 17, No. 4, 272–8, 1 fig. [21 refs.]

A survey of respiratory symptoms and function was made in Dundee among 123 jute workers, 242 flax workers and 72 men in a heavy engineering firm—in all, 316 men and 121 women. Chronic bronchitis (defined as cough with sputum persistent through the winter for at least two years in the absence of other causative respiratory disease) was found in 82 men and 14 women—a highly significant difference between the sexes. Differences in bronchitis prevalence between the industries were not significant. Byssinosis was diagnosed in 38 persons, all of whom were flax workers. In addition, 35 persons employed in flax gave a history of cough alone, which was worse on Monday. The average ventilatory function of the flax workers was no worse than that of the other workers. However, the characteristic fall in forced expiratory volume, which occurs in cotton workers [this *Bulletin*, 1958, v. 33, 854], was found in flax workers on Mondays but only in

those who had symptoms of byssinosis. Byssinosis in flax workers is not closely related to length of time of exposure to flax dust and so far no evidence has been found that it produces any serious disability. It is a milder disease than that described in cotton workers.

R. S. F. Schilling

TUFFNELL, P. **The Relationship of Byssinosis to the Bacteria and Fungi in the Air of Textile Mills.** *Brit. J. Indust. Med.* 1960, Oct., v. 17, No. 4, 304–6.

The author studied the relationship between the concentration of live organisms in the air and the prevalence of byssinosis in 2 cotton and 2 jute mills. The concentrations of viable micro-organisms in the cardroom of all four mills was very high, whereas the prevalence of byssinosis was high in only one mill (72 out of 135 persons at risk). No association was established between the total concentration of live micro-organisms in the atmosphere and the prevalence of byssinosis but there was an association between prevalence and the number of live organisms of *Bacillus pumilus* and *B. subtilis*, which led to the next investigation [below] of exposing, under controlled conditions, byssinotic subjects to the genus *Bacillus*.

R. S. F. Schilling

TUFFNELL, P. **Experimental Byssinosis.** *Brit. J. Indust. Med.* 1960, Oct., v. 17, No. 4, 307–9, 1 fig.

5 men with byssinosis and 2 with bronchitis were exposed under laboratory conditions on separate occasions to the following types of dust:—

calcium carbonate, *Bacillus pumilus*, *Aspergillus niger*, cotton plant leaf, and cotton mill dust.

The concentrations of the dusts varied from 180 to over 900 particles per ml. (measured with a thermal precapitator) and the viable organisms from 1,510 to 12,700 per cu. ft. (measured with a slit sampler). 1 man's reactions to leaf and mill dust was pronounced and exactly resembled his symptoms when working in the mill. 2 other men with moderately severe byssinosis did not experience any characteristic symptoms but one had a reduced forced expiratory volume after exposure to leaf and mill dusts. The 2 men with chronic bronchitis and the 2 with mild byssinosis symptoms had no particular reaction except that those with bronchitis reacted slightly and similarly to all the dusts.

R. S. F. Schilling

SMILEY, J. A. **Background to Byssinosis in Ulster.** *Brit. J. Indust. Med.* 1961, Jan., v. 18, No. 1, 1–9, [31 refs.]

The linen trade in Ireland was flourishing in the 13th century and remained a cottage industry until quite late in the 19th century.

The Industrial Revolution had scarcely touched Ireland by the time it was reaching its crescendo in Lancashire, because low wages made mechanization hardly worth while. In the latter half of the 19th century Ulster became aware of a severe respiratory disease in the dusty processes in linen mills. Army surgeons forbade recruiting sergeants to enlist flax dressers and there is good epidemiological evidence of this respiratory hazard from the dispensary attendances. 18·7% of the mill workers, but only 6% of all the workers had diseases of the chest. Later PURDON gave more details of the ravages caused by inhaling flax dust. OLIVER named this chest disease of textile workers byssinosis, after the Greek word for fine flax. At the beginning of the present century interest waned in byssinosis, probably because of a general improvement in working conditions.

Less than 15 years ago the author recognized the disease in Belfast hemp and flax spinners and gives histories of 4 typical cases. There appears to be some reluctance in Northern Ireland to accept the fact that byssinosis still does occur in flax mills in spite of improved conditions. An epidemiological survey is needed to determine its prevalence.

R. S. F. Schilling

DEGUELDRE, G. & VANSTRAELEN, M. La lutte contre les poussières dans les charbonnages belges. Situation au début de l'année 1960. [**Dust Suppression in Belgian Coal-Mines. Position at the Beginning of 1960**] *Rev. Inst. Hyg. des Mines.* Hasselt. 1960, v. 15, No. 4, 147–65.

This paper presents statistics showing the extent to which the various methods of dust suppression were being applied in Belgian coal mines at the beginning of 1960. The statistics, set out in tabular form, show for each coalfield the numbers of mining companies that are applying various methods of dust control, and for comparison the results of enquiries made in 1954 and 1958 are also given. Since 1954 the number of companies applying water infusion at the coal face has increased from 18 to 30.

Statistics of the lengths of coal faces treated by prespraying, wet cutting, water infusion, and wet pneumatic picks are given. On 45·6% of the coal faces one or other of these methods is applied, including 31% where the faces are infused with water. On 7·9% of the faces 2 of these treatments are applied in combination; on 18·6% one of these methods is combined with the use of mist projectors, and on 23·8% mist projectors only are used. 30·6% of the faces are untreated. On 13·8% of these there is little dust owing to the natural moistness of the mines, but means of dust prevention are still required on the remaining 16·8%.

Thomas Bedford

STEVENS, D. C. & HOUNAM, R. F. **A Fine Glass Fibre Paper for Air Sampling.** *Ann. Occup. Hyg.* London. 1961, Jan., v. 3, No. 1, 58–63, 7 figs. (4 on 4 pls.).

"A thin, low-density paper made from very fine glass fibres has recently become available. It combines a low

resistance to airflow with high collection efficiency for aerosols. Its advantages compared with filter papers previously used for air sampling for particulate contamination are briefly described with particular reference to the problems of sampling radioactive aerosols."

ŠIMECEK, J. & VONDRÁCEK, V. Vlastnosti a použití membránových filtrů "Synthesia". **[The Properties and Use of Membrane Filters "Synthesia"]** *Československ. Hyg.* Prague. 1961, v. 6, No. 1, 46–54, 3 figs. & 3 graphs. English summary (8 lines).

The authors mention various methods of measuring the quantity of dust in the air; some use electrostatic precipitation, others thermoprecipitation and also sedimentation. They claim that none of these methods are reliable or give uniform results. To estimate the total amount of aerosol in the atmosphere it is necessary to have a standard method which will separate all particles of biological importance with the help of a simple, cheap and easily portable apparatus. They found that the only one which would comply with these basic requirements was the membrane ultrafilter (MF) Synthesia.

A sample of aerosol obtained on an MF can be analysed in many ways:

(1) by weighing the gravimetric unit of dust (mgm/m^3) can be established;

(2) microscopic examination reveals the particle concentration (particles/cm^3);

(3) by electron-microscopy particles invisible in an ordinary microscope (under 0·44 μ) can be distinguished;

(4) mineralogical analysis;

(5) direct chemical analysis by special impregnation of the MF so that H_2SO_4, HNO_3 and others can be easily detected.

The pores of the filter are homogeneous, the average size being 0·8 μ. Particles which are absorbed do not coagulate, nor do they break up as in other filters. For experimental use or routine purposes the MF can be prepared in various colours.

The head of the MF consists of two basic parts and a metal support for the actual filter membrane. The filters manufactured at the moment have pores varying from 0·3 to 0·6 μ and 0·6 to 0·9 μ MF with pores from from 0·1 to 0·3 μ and 0·9 to 1·2 μ are being developed. Filters are also available in the following sizes: 24, 35, 60, and 100 mm.

The MF was tested for its resistance, which was found to be very low (about 20 mm. Hg), needing a correction of only about 3%.

MF filters are not hygroscopic. Homogeneity is tested during production by a constant flow of distilled water. The filter is elastic and even when bent 180° will not break.

To avoid "peeling" of the layer of dust it is suggested that the maximum amount of dust on 1 cm.^{2} should not exceed 1·5 mgm.

The authors believe that this method of MF can still be further developed and improved and that by establishing a standard technique a universal method may be developed. *Paul Frankl*

BUGDEN, A. R., HAMILTON, R. J. & JONES, G. H. S. **Application of Photoelectric Densitometry to the Assessment of Respirable Dust Samples.** *Brit. J. Applied Physics.* 1960, Aug., v. 11, No. 8, 371–7, 9 figs. [11 refs.]

The Thermal Precipitator (TP) is the standard instrument for sampling respirable dust in coal mines in the United Kingdom but suffers from the disadvantage that both sampling and the visual counting of samples are tedious and subject to errors. Some years ago HAMILTON [this *Bulletin*, 1957, v. 32, 258] described a long-running TP (LRTP) which greatly reduced the labour in collecting samples: the present paper describes a method of assessing the samples taken with the LRTP without visual counting.

The object of the assessment is to express the deposit on the slide as a number concentration of particles within the respirable range in the original cloud. To do this the authors use the fact that the LRTP separates the particles by size gravitationally, and have designed a mask to superimpose on the deposit, which divides it into 12 narrow strips each containing particles all about the same size. The areas of these strips which the mask leaves exposed are inversely proportional to the effective cross-sectional areas of particles in the corresponding size-ranges, so that the numerical concentration can be estimated from the light passing through the combination of deposit and mask. The densitometer used for measuring the transmission is described, and results of comparisons of densitometric and microscopic counts on laboratory calibration samples and on routine mine samples are given. The calibration factors extend to 1 micron diameter only: it is impractical to use it for smaller particles as these are precipitated thermally and there is no separation by size.

The method described is an extremely valuable simplification of standard procedure, but it should be noted that a given mask will only suit a particular dust: the profile of the mask will depend on the effective density of the dust. *J. McK. Ellison*

MIURA, T. & KIMURA, K. **On the Allowable Limit of the Air Flow Resistance of Respirator.** *Rep. Inst. Sci. of Labour.* Tokyo. 1960, Nov., No. 57, 1–9, 16 figs.

An apparatus, incorporating a strain gauge on a diaphragm, records the pressure changes inside the facepiece of a respirator. Experiments with subjects working a bicycle ergometer revealed that the maximum air flow during respiration could rise to 4 times the average calculated from the minute volume. The resistance of a respirator rated at 10 mm. water gauge on inspiration and 2·5 mm. on expiration, with the normal steady test flow of 30 litres per minute, rose to maxima of 100 mm. on inhalation and 50 mm. on exhalation, and the subjects complained of difficulty in breathing.

It is suggested that a limit of 60 mm. water gauge resistance at the peak flow rate on inhalation should not be exceeded. *C. N. Davies*

ELKINS, H. B. **Maximum Acceptable Concentrations. A Comparison in Russia and the United States.** *Arch. Environment. Health.* Chicago. 1961, Jan., v. 2, No. 1, 45–9. [13 refs.]

Maximum Acceptable Concentrations (MAC) recommended in Russia are given for 49 substances not listed elsewhere, and also for over 100 which, with few exceptions, are shown to be very much lower than the widely accepted values recommended by the Threshold Limits Committee of the American Conference of Governmental Industrial Hygienists. Though lower MAC for some substances have been suggested by other European organizations, none are as low as the Russian. Many of the Russian MAC are based on animal physiological data, *e.g.*, of the sensitive conditioned reflex type. American MAC were originally based on such experimental animal criteria as death or changes in body or organ weight, and are revised each year in the light of experience. It appears that the Russian values are enforced for new factories, but not, in all cases, in the old ones. This may imply that conventional methods cannot meet the MAC in all processes, as indeed would be predicted by those familiar with many processes such as those involving *e.g.*, mineral dust, lead dust or fume and carbon monoxide. While Russian MAC for chlorinated hydrocarbon solvents are very low, those for most organic dusts and fumes, which include chlorinated hydrocarbons, agree well with the American; 3 of the insecticides have lower MAC in Russia. [See also this *Bulletin*, 1960, v. 35, 434.]

M. Patricia Fitzsimons

MORRILL, E. E., Jr. **Tetraethyl Lead Poisoning Incident with Eight Deaths.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 515–17, 1 fig.

This was caused by lack of constant supervision while aviation leaded-petroleum tanks were being cleaned even though the contractor had previous experience and though he and his workmen were trained by United States Army safety personnel who specified methods and equipment necessary for safety and health. Another reason, found when 23 men became ill, was that these men who had spent 5 months cleaning the tanks thought that the absence of odour and the lower explosiometer tests in the 6th and largest tank meant that it was safe. This was built underground before the war by the Japanese, with steel walls, concrete floor, diameter 125 feet, depth 95 feet, a 4-foot manhole and a smaller vent at the top and the petroleum inlet at the bottom.

The tank was drained and flushed with sea-water. Sea-water was pumped in to the top to expel vapour and support rafts for the workmen, who wore life-jackets, protective clothing and compressed-air respirators. The water level was lowered as the walls were cleaned by means of high-pressure streams of water. Sludge from the bottom was scraped wet into drums which were hoisted out of the manhole. The sludge was transferred to an open handcart and wheeled to a pit 150 feet away.

The contractor was warned when he and some workmen did not wear their respirators and he dismissed some. The equipment was in good order though some gloves and boots had been patched. The workmen who died had all handled sludge, but the contractor, though only in the tank for short periods, also died. In the differential diagnosis, botulism, Japanese B encephalitis and poisoning by methyl alcohol, narcotics, insecticides or chemically contaminated food containers were excluded. The only common factor was exposure to tetra-ethyl lead, the illness was typical and the lead content of blood and urine was high.

M. Patricia Fitzsimons

SMITH, J. C., WELLS, Agnes R. & KENCH, J. E. **Observations on the Urinary Protein of Men exposed to Cadmium Dust and Fume.** *Brit. J. Indust. Med.* 1961, Jan., v. 18, No. 1, 70–78, 2 figs. [30 refs.]

It is known that those exposed to cadmium fume or dust exhibit marked proteinuria [this *Bulletin*, 1956, v. 31, 295; 1958, v. 33, 484]. This paper describes electrophoretic behaviour and chemical analysis of the various components of the cadmium urinary protein. The 5 men studied were all excreting protein in quantities greater than 1 gm. per litre. The methods by which the urine was analysed, including the techniques for elucidating the electrophoretic behaviour of the protein, are described. Filter paper electrophoresis showed a preponderance of globulins over albumin, but column electrophoresis showed a higher proportion of albumin. Explanations are offered for this. The distinctive feature of the proteinuria appears to be the presence of a low molecular urinary albumin, the origin of which is being further investigated.

T. O. Garland

LAWSON, J. J. **The Toxicity of Titanium Tetrachloride.** *J. Occup. Med.* Chicago. 1961, Jan., v. 3, No. 1, 7–12, 2 figs.

A corrosive liquid which reacts violently with water to liberate heat and HCl: such is $TiCl_4$, which fumes in moist air. Emergency treatment of splashes should be taught to operatives, if chemical burns are not to be made worse by instinctive flushing with water. After a splash on a full acid-protective suit, the heat generated under a shower forced the wearer to pull off the clothing, with a consequent third degree burn of the hand. Deep brown pigmentation near burns treated with water suggested entry of a reaction product through intact skin. Similarly, pulmonary damage after inhalation of fume may be due to slow liberation of oxides or oxychlorides resulting from hydrolysis, as well as HCl.

Permanent damage to the eye follows a splash or severe fume exposure. The surrounding skin must be wiped dry before eye-irrigation with cold water. Then particles of dioxide or oxychloride should be removed. Prolonged irrigation should follow with isotonic saline solution, and not with bicarbonate solution.

Preliminary wiping with dry material is essential for splashes. Wiping material should be available in sealed moisture-proof polyethylene bags. Residual deposit should be removed with cold water. Burns so treated heal well. This treatment of volunteers who applied

anhydrous $TiCl_4$ to dried forearm skin and let it remain for 1 minute, resulted in no lesions or discomfort except stinging which stopped on washing.

Acute and chronic exposure to fume are described. Data of 10 subjects, exposed to low concentrations for at least 4 years, show no abnormalities or symptoms except as follows. A few had eosinophilia or relative lymphocytosis; 1 man's vital capacity was 78% of normal; another's chest X-ray showed left basal fibrotic and infiltrative changes which remained stationary for 10 years.

Air-line masks are necessary when exposure to fume may occur. Those working nearby should carry escape respirators. Exposure to fume should be treated by immediate oxygen administration for at least 20 minutes and bed-rest for at least another hour.

M. Patricia Fitzsimons

MIKISKA, A.; MIKISKOVÁ, H. Bestimmung der elektrischen Erregbarkeit der motorischen Grosshirnrinde und ihre Verwendung in der Pharmakologie und Toxikologie. I. Mitteilung. Methodik, Kontrollversuche und physiologische Grundlagen [**Determination of the Electrical Excitability of the Motor Cerebral Cortex and its Use in Pharmacology and Toxicology. Part I. Method, Control Investigation and Physiological Basis**] [MIKISKA]. *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 3, 286–99, 4 figs. [Numerous refs.] II. Mitteilung. Wirkung von Benzol, Toluol und Xylol bei Meerschweinchen [**Part II. Effect of Benzol, Toluol and Xylol on Guineapigs**] [MIKISKOVÁ]. *Ibid.*, 300–309, 6 figs. [27 refs.] III. Mitteilung. Vergleich der narkotischen Wirkung von Trichloräthylen und Trichloräthanol bei den Meerschweinchen [**Part III. Comparison of Narcotic Effect of Trichloroethylene and Trichloroethanol in Guineapigs**] [MIKISKOVÁ & MIKISKA]. *Ibid.*, 310–16, 3 figs. [12 refs.]

I. Previous literature has shown that narcotic agents lower the excitability of the cerebral cortex, as shown by a raising of the threshold of stimulation, while convulsive stimulation begins at a tension level 20 to 25% higher than the recorded threshold value.

This article describes a method which it is claimed is suitable for the study of the time interval in pharmacological research and is capable of adequate standardization. Rabbits and guineapigs are used, but for closer localization, cats, dogs or apes are necessary.

The method involves the use of epidural electrodes for alternating current, the skull being trephined. Needle electrodes fixed to the bone can also be used with rabbits, and give a threshold value 2 to 3 times higher than with the epidural, but are not suitable for guineapigs owing to possible penetration of the thinner bone.

Threshold values are estimated from the level at which with repeated stimulation muscle contraction does not disappear, the average being calculated from a series of 6 estimations made every 5 minutes. In most of the experiments the contraction of the forelimbs was observed visually, in others by an electromagnetic colour recorder. Variation in the threshold level of the experimental animals closely resembled that of the "spontaneous" variation of the controls (−6 to+5%); outside these limits the variation is statistically significant.

The physiological basis of the estimation is complicated by the fact that neurons excited by the current are connected by synapses, and therefore the stimulation is distributed over a wide field, a sufficiently strong impulse resulting in a series of impulses in the corticospinal nerve fibres. Co-ordinated movements indicate a simultaneous inhibition of antagonists, thus differentiating cortical excitability from that of peripheral nerves and muscles.

Rhythmic impulses show a much smaller influence of summation than single impulses. If rhythmic stimulation 50 to 100% above the threshold level is continued for several seconds, a strong epileptiform condition is produced; this is known as the "convulsive threshold".

The cortical motor threshold depends therefore on the nature of the current, the duration and repetition of stimulation and the most important reflexes such as central regulation of the vegetative system; these must be considered in relation to prevention of false results.

II. The raising of the threshold of excitability of the motor cortex can be regarded as a measure of the depth of narcosis, or narcotic effect. The method used for comparison of the narcotic effect of benzol, toluol and xylol was that described in Part I with guineapigs as experimental animals.

Controls given 0·4 ml. of physiological saline intraperitoneally showed a threshold variation not greater than 5–6% as compared with those without injection, indicating that intraperitoneal injection alone had no influence on the threshold level.

Benzol, toluol and xylol (a commercial mixture of all 3 isotopes) were given in doses of 0·6 ml. per kgm.

Benzol gave in a few cases a rise, in others a fall, of the threshold, with the greatest variation 3 hours after injection, but the average increase was not significant. Toluol and xylol gave a greater increase, but with xylol there was an earlier return to a normal level.

It was concluded that the narcotic effect rose sharply in the series of homologues. Clonic muscle contractions and tremor were observed in a few animals with xylol and in all with benzol, but not with toluol. These effects are not comparable with those of typical narcotics, but indicate, in agreement with the results of previous investigators, that acute poisoning by the aromatic hydrocarbons shows itself in two phases—inhibition or narcosis, followed by increased excitability with a lowering of the cortical motor threshold and by behaviour changes in the animals. The narcotic phase is of short duration and increases from benzol to xylol.

Estimation of the cortical excitability threshold is suitable for evaluation of the toxic effect on the central nervous system but this is not directly influenced by injury of the internal organs.

III. Acute trichloroethylene poisoning is accompanied by excretion of trichloroacetic acid and trichloroethanol, the latter in 8 times the amount of the

former. Clinical symptoms are most severe when urinary trichloroethanol is greatest, while recovery from coma occurs during the maximal excretion of trichloroacetic acid.

It has not hitherto been decided whether trichloroethylene itself or its metabolites are responsible for its toxicity. This investigation attempts to assess the relative narcotic effect of trichloroethylene and its metabolites by estimating the threshold of excitability of the motor cortex of guineapigs, with epidural electrodes and alternating current.

Trichloroethylene, in a dosage of 0·2 ml. per kgm. by intraperitoneal injection, gave a variation, in only 2 series out of 6, of 9% above the normal, but in a dosage of 0·6 ml. per kgm. an average of 13 to 16% above normal. The greatest increase occurred 3 hours after injection, indicating a greater narcotic effect due to the metabolites. Trichloroethanol, in a dosage of 0·65 ml. per kgm., was followed in 2 to 3 minutes by deep narcosis, in which the motor cortex was unexcitable; a few minutes later the corneal reflex disappeared and within half an hour the animals died from respiratory paralysis.

With a dosage of 0·22 ml. per kgm. all animals showed deep narcosis, with its highest point 5 to 30 minutes after injection. Increase of the current to 12 V did not cause muscle contraction. Depth of narcosis decreased after 60 to 90 minutes and recovery was accompanied by severe subacute symptoms; the threshold level fell during the deepest narcosis.

Electro-encephalograms showed slow irregular waves of large amplitude; the basic rhythm was re-established 60 to 90 minutes after injection, but the electro-encephalogram was still not normal after recovery from narcosis.

In contrast to aromatic hydrocarbons, no lowering of the cortical motor threshold of excitability was observed with trichloroethylene. This, together with the muscle relaxation, side position and absence of tremor, twitchings and convulsions, indicated that trichloroethylene has a typical narcotic effect.

Comparison of its threshold value with that of trichloroethanol shows that the latter has a narcotic effect greater than that of 3 times the dose of trichloroethylene. The cause of the lowering of the threshold after disappearance of narcosis with a dosage of 0·22 ml. per kgm. of trichloroethanol remains unexplained, and it was not possible to state whether the subacute symptoms were due to injury of the central nervous system or of parenchymatous organs.

It is concluded that trichloroethanol plays an important role in the pathogenesis of trichloroethylene poisoning. *Ethel Browning*

URANUMA, T. **[An Experimental Study on a Toxicity of Dimethyl-Sulfoxide as a Solvent]** *Igaku Kenkyu.* Fukuoka. 1960, Aug., v. 30, No. 8 (Extra Edition) 2235–61, 11 charts and 18 figs. [40 refs.] [In Japanese.] English summary.

Dimethyl sulphoxide is a solvent for synthetic fibre and synthetic resin; it is in common use. The author exposed mice to it by injecting it subcutaneously (the LD50 was 25–64 mgm. per gm. of body weight) either in a single large dose or continuously for up to 241 days. The dosages are unfortunately not explicit in the English summary but it seems that some mice were given 0·1 cc. and some 0·05 cc. In other mice 0·02 cc. was painted daily on the back, the fur being either cut or uncut. The mice which received injections showed evidence of pneumonia, parenchymatous changes in the liver and kidneys, but some lived for up to 203 days.

Rabbits "serially inhaled 50 cc. an hour" of dimethyl sulphoxide mist [the dispersion of the chemical in the inhaled air is not detailed, and the duration is not given, in the English summary]. It is said that *mice* showed corneal opacity, and 2 of 4 died, after inhalation, showing pneumonia and slight changes in liver, kidneys and spleen.

Dimethyl sulphoxide is said to be among the least poisonous of solvents, but the author comments that inhalation of large amounts is dangerous.

Charles Wilcocks

FUGISAKI, K. **[A Study on a Toxicity of Dimethyl-Formamide as a Solvent]** *Igaku Kenkyu.* Fukuoka. 1960, Aug., v. 30, No. 8 (Extra Edition) 2291–324, 8 charts & 28 figs. [54 refs.] [In Japanese.] English summary.

Dimethyl formamide is a solvent used in association with synthetic fibres and synthetic resins. The LD50 on subcutaneous injection in mice was 5·07 mgm. per gm. body weight, and acute poisoning by this route resulted in lesions of the central nervous system and cardio-respiratory system, with cramp, dyspnoea and death. Pneumonia and cloudy swelling of the liver were also seen.

After subcutaneous injection of 10% or 4% of the LD50 daily for 3 months the animals remained healthy, though on post-mortem examination slight changes were observed in lungs and liver. 0·02 ml. was painted daily on the skin (denuded of fur), and 45% of the mice were alive after 90 days, but there was weight loss and emaciation. There was no local change at the site of application, but inflammation was seen in the lungs and necrosis in the liver, with erosion and ulcers in the stomach and intestines.

Mice received 0·2 ml. or 0·05 ml. daily by mouth and all the first (0·2 ml.) group died in 20 days; 50% of the 0·05 ml. group were alive at 40 days. Post-mortem changes resembled those of mice given the solvent by application to the skin. *Charles Wilcocks*

HOME OFFICE. **Fumigation with Methyl Bromide. Precautionary Measures, 1960.** 8 pp. 1960. London: H.M. Stationery Office. [6d.]

The penetrating power of this highly toxic fumigant; the absence of smell; the latent period, 1–24 hours or more between exposure and what may be a long serious illness; the deaths from continued or repeated exposures to low concentrations as well as from a heavy exposure: these facts make esential precautions at all stages, from manufacture to the certificate of freedom from danger at the conclusion of operations. Danger must be

prevented in spaces adjoining the sealed fumigation enclosure, *e.g.*, alleyways, shafts and particularly in ships and time given for absorbent material to become free of the gas. Extra responsibility is thrown on the operator in charge of fumigating, and this implies at least 2 trained operators.

Methyl bromide cylinders should comply with British Standard Specification No. 401 and have valves complying with B.S.S. No. 341 subject to certain conditions specified in this pamphlet. Joints and unions should be tested by means of a halide detector lamp, irrespective of the lachrymatory indicator sometimes added by the manufacturer to warn of gross leaks. Quantitative tests may be necessary. A concentration of 20 p.p.m. is usually safe. High concentrations may form at floor level. Self-contained or distance breathing apparatus should be used in high concentrations. For short periods in concentrations not exceeding 1%, methyl bromide canister respirators have been approved by H.M. Chief Inspector of Factories. Cylinders should never be manually operated in the enclosure.

First-aid organization includes a supply of gassing casualty labels or medical guidance notes obtainable from the manufacturer or the Association of British Chemical Manufacturers. Clothing splashed by liquid should be removed—and the skin washed—or burns will develop from the vapour; the liquid evaporates from bare skin. Symptoms of poisoning include lethargy, dim or double vision, headache, staggering, vomiting or convulsions. If exposure is even suspected the person should be sent to hospital by stretcher with the notes.

M. Patricia Fitzsimons

RATHUS, E. M. & LANDY, P. J. **Methyl Bromide Poisoning.** *Brit. J. Indust. Med.* 1961, Jan., v. 18, No. 1, 53–7. [24 refs.]

40 men were engaged in fumigating a large housing estate in Queensland with methyl bromide to eradicate borer. Each house was covered with heavy duty polythene sheeting and the gas was then run in from cylinders. All 7 cases of poisoning here described occurred in men removing the sheeting and clearing the houses for ventilation after fumigation. The first occurred on April 30, 1958, and afterwards safety precautions were tightened up, but there were further cases on May 29, July 1 and 4 on July 25. At this point doubt was cast upon the efficacy of the gas canisters fitted to the masks. On testing none of them was found to protect against methyl bromide for longer than 30 seconds.

Brief notes on the cases are given. 5 of the 7 had major epileptiform seizures and 2 had periods of unconsciousness lasting several days. Gross ataxia and Jacksonian motor attacks of right leg have persisted in Case 1, and epileptic attacks in Case 2. In each case mentioned there was a latent period between exposure and the onset of neurological symptoms. All were treated with BAL. In 2 cases large doses of intramuscular phenobarbitone and intravenous myanesin were required to control the fits.

The method of testing the canisters is described and it is recommended that as part of the supervision of workers using methyl bromide periodic estimation of blood bromide by the micro-diffusion method of Cowdray be mandatory. There is a short discussion of the action of methyl bromide on the central nervous system.

T. O. Garland

MALCOLM, D. & PAUL, E. **Erosion of the Teeth due to Sulphuric Acid in the Battery Industry.** *Brit. J. Indust. Med.* 1961, Jan., v. 18, No. 1, 63–9, 6 figs. [14 refs.]

These studies were undertaken in the forming and charging departments of a battery manufacturing plant where the acid mist expressed as pure sulphuric acid varied from 3 mgm. to 16·6 mgm. per cu.m. of air.

The teeth of men working in these two departments were compared with a control group and full clinical details of damage to the teeth are given. Far more men were affected in the forming room where the strength of the acid mist was higher than in the charging room. The teeth affected are invariably the centrals and laterals on their labial surfaces—canines were affected to a much lesser extent. Teeth beyond the canines, where the lips provide a shield, were never damaged. None of the men with etching or erosion had experienced pain or sensitivity at any stage. The degree of erosion was usually directly related to length of exposure and strength of the acid mist. It was apparently uninfluenced by oral hygiene or dental caries. Attempts that have been made to protect the workers are described briefly. Improved general ventilation is the most successful—alkaline mouth washes give no lasting protection and teeth shields are not tolerated.

Other acids producing similar dental changes are hydrochloric, nitric and tartaric but not hydrofluoric acid.

T. O. Garland

GERARDE, H. W. **Toxicological Studies in Hydrocarbons. VII. A Gravimetric Method for the Determination of Inorganic and Ethereal Sulfate in Urine.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 511–14, 3 figs.

Estimating the ratio of inorganic to total sulphate in a 50 ml. urine sample for a test of exposure to benzene took a chemist at least 4 hours. The simple method now described, and illustrated, enables a technician to estimate 12 samples of 10 ml. in less than 4 hours.

Hydrolysis of the organic sulphate is shortened by autoclaving 5 ml. urine and 5 ml. 6N HCl in the total-sulphate (T) bottle. A rapid pressure filtration technique, by means of a cotton-tipped wood applicator fitted closely into the plastic filter top screwed on the bottle after adding a sodium bicarbonate tablet, enables filtration into a tared centrifuge tube to be completed in a few minutes. To this tube the barium chloride solution is added, and in it, after centrifuging, washings are done and the final deposit is dried, slow ignition not being necessary since carbonaceous material had been removed by filtration before the addition of the

barium salt. A similar process, without autoclaving, is carried out in the inorganic-sulphate (I) bottle while the T bottle is in the autoclave.

A ratio (I × 100)/T above 80 means negligible—normal exposure, a ratio below 70 is dangerous: I and T are weights in mgm. of the deposited barium sulphate in the unhydrolysed and hydrolysed portions respectively. If the urine in the I bottle remains clear after acidification, filtration is not necessary, but in this case I in the ratio calculation is larger than T by about 1% since liquid hold-up errors in the 2 bottles during filtration do not cancel out: this can be overcome by washing the T bottle with HCl and filtering again. The method has been used successfully for 2 years.

M. Patricia Fitzsimons

AUBERTIN, X. Intoxications par l'acide cyanhydrique et ses dérivés; leur thérapeutique d'urgence. **[Poisoning by Hydrocyanic Acid and its Derivatives; Emergency Treatment]** *Arch. Malad. Professionnelles.* Paris. 1960, Oct.–Nov., v. 21, Nos. 10/11, 643–51.

The treatment advocated does not altogether conform with classical methods; the reasons are given during a full account of HCN poisoning, and depend upon Professor A. G. PAULET'S experiments with dogs. Manufacture of HCN, acetone cyanhydrin, acrylonitrile and methylmethacrylate are briefly mentioned, the last 2 not causing true cyanide poisoning.

Acute poisoning—as distinct from immediately fatal poisoning—is considered as 4 artificial phases: stimulation, polypnoea; depression, irregular respiration and apnoea; convulsions; paralysis. Convulsions have also appeared early or when the patient is coming out of coma. Since HCN leads to asphyxia, the important signs to note are respiration, pulse and blood pressure. For treatment poisoning is classified as: light, no loss of consciousness; serious, coma, normal breathing; grave, coma, arrested breathing.

First-aid workers are instructed to administer oxygen immediately in all cases, and if breathing has stopped by means of a machine and artificial respiration. No amyl nitrite, analeptics, cardiac stimulants, friction or hot-water bottles are allowed. Movement must be prevented and the patient protected against cold.

Guidance for doctors is based upon general principles. Treatment should be decided upon according to the respiration and cardiovascular signs, and the route of absorption. For serious poisoning, oxygen should be continued and serum glucose containing vitamins B and C injected. For grave poisoning, treatment, in addition to oxygen, depends on 2 states. If the pulse is strong and the blood pressure above 70 mm. sodium nitrite followed by sodium hyposulphite is advised. If the pulse is weak and the pressure lower, rapid intravenous injection of a chelate of cobalt is advocated. This has not been used in man but has resuscitated dogs. When fit to be moved, the patient should be kept in hospital, given oxygen, glucose infusions and supportive therapy, and observed for some days for possible rare neurological sequelae.

M. Patricia Fitzsimons

CHAUMONT, A. J. & WEIL, E. Intoxications mortelles par cyanures à l'atelier. **[Fatal Cyanide Poisoning in the Workshop]** *Arch. Malad. Professionnelles.* Paris. 1960, Oct.–Nov., v. 21, Nos. 10/11, 657–60.

Elementary care would have prevented the 2 deaths described. Autopsies, performed without delay, and analysis of organs, described in detail, showed HCN poisoning by inhalation and ingestion. Emphasis is given to the paradox by which such negligence is permitted whereas legislation stringently covers the care of dangerous chemicals by pharmacists.

A man aged 50 was given a sponge and a bucket containing 15% sulphuric acid to clean an electroplating bath. This had been emptied the day before and turned on its side. He was found dead 7 minutes later with his face on the under side. Calculations show that the acid released between 60 and 120 times the lethal dose from residual solution and cyanide crystals deposited on the walls. The bath should have been rinsed out the day before, and the man provided with hose-pipe and water. He was not warned of any danger.

A girl aged 16 was employed in applying a harmless paste to cloth in a silver-coating workroom. She went home to lunch and later during the lunch break she was seen walking away from the workroom when she fell unconscious. She died 30 minutes later. The workroom was always empty and unlocked during the lunch hour; a long-handled mixing ladle was beside the cyanide bath: this knowledge and opportunity facilitated her suicidal impulse.

M. Patricia Fitzsimons

CHAUMONT, M. A. J. L'intoxication chronique par les cyanures et l'acide cyanhydrique. **[Chronic Cyanide and Hydrocyanic Acid Poisoning]** *Arch. Malad. Professionnelles.* Paris. 1960, Oct.–Nov., v. 21, Nos. 10/11, 660–62.

This short account of an illness was presented after a review of the various symptoms and signs which have been described in workers exposed to HCN or cyanides to illustrate the common difficulty of legislating for non-specific symptomatology which on circumstantial evidence is considered occupational in aetiology. The patient, aged 48, began to complain of vomiting, giddiness, cold sweats and straining (*tenesme*) 3 months after changing from chromium plating where ventilation was good to brass plating in small baths where there was no exhaust ventilation. Reddening and atrophy of the nasal mucosa was noted, and some deviation of the outstretched arms and Rombergism. The urine contained a trace of albumin, red blood cells and leucocytes. He was admitted to hospital 7 weeks later for 10 days. The discharge report stated that he had been admitted for cyanide vapour poisoning, that functional symptoms had disappeared as soon as he had left the harmful atmosphere and that no organic lesion was found. He had worked with cyanides of zinc, copper and potassium and chromic acid for 4 years. Compensation was not granted. Though the existence of chronic cyanide poisoning is not deniable, repeated subacute poisoning

is more likely. However, such discussions do not solve the problem for the affected worker.

M. Patricia Fitzsimons

HINE, C. H., GUZMAN, R. J., DUNLAP, M. K., LIMA, R. & LOQUVAM, G. S. **Studies on the Toxicity of Glycidaldehyde.** *Arch. Environment. Health.* Chicago. 1961, Jan., v. 2, No. 1, 23–30.

In order to assess the degree of "radiomimetic" hazard [see KODAMA *et al.* p. 539] rabbits were intravenously injected with 100, 50 or 25 mgm. per kgm. glycidaldehyde, and other rabbits and 2 dogs were given 25 mgm. per kgm. intravenously each week for 4 weeks. Groups of 10 rats were exposed for 4 hours a day on 5 days a week for 12 weeks to 10, 20, 40 or 80 p.p.m. Previous range finding toxicity data show that the oral LD50 of glycidaldehyde in the rat is 232 mgm. per kgm. and the LC50 is 252 p.p.m., and that the rabbit percutaneous LD50 is 249 mgm. per kgm. Glycidaldehyde, an oxidized form of acrolein, is an irritant. In toxic doses it caused convulsions, miosis with congestion of the iris, lachrymation, salivation, pulmonary irritation and occasionally damage to liver, kidney and testis. Rabbits intravenously injected with 1 or 2 mgm. per kgm. mechlorethamine HCl, as positive controls, were less severely affected but blood changes were greater.

Single injections of 25 and 50 mgm. per kgm. glycidaldehyde altered leucocyte morphology. Repeated injections caused leucopenia and neutropenia in the rabbits but not in the dogs. At 10 p.p.m. the rats showed only diminution of the thymus; at 20 p.p.m., with 1 death, weight gain was retarded and nucleated marrow cells were decreased; at 40 p.p.m., with 2 deaths, the spleen was small; at 80 p.p.m. the 2 survivors in addition had a reversed polymorphonuclear/mononuclear ratio, but no leucopenia.

Glycidaldehyde has mild "radiomimetic" properties and warning irritant properties. In 5-minute sensory threshold tests, odour was recognized at 1 p.p.m. with eye and nose irritation. Sneezing occurred at 5 p.p.m., pulmonary discomfort became severe at 10 p.p.m. and mild headache appeared at 20 p.p.m. A threshold limit of 2 p.p.m. is suggested. *M. Patricia Fitzsimons*

HINE, C. H., KODAMA, J. K., GUZMAN, R. J., DUNLAP, M. K., LIMA, R. & LOQUVAM, G. S. **Effects of Diglycidyl Ether on Blood of Animals.** *Arch. Environment. Health.* Chicago. 1961, Jan., v. 2, No. 1, 31–44.

Diglycidyl ether (DGE) was tested further and compared with triglycidyl phosphate (TGP) and epoxy resin A [see KODAMA *et al.* p. 539]. Rats, rabbits or dogs were given some of the compounds in various doses by single or repeated administration by skin application, intravenous or intramuscular injection or inhalation. DGE caused "radiomimetic" effects by all routes. Similar effects were obtained by TGP, which was given only by intravenous injection to rabbits and 1 of 9 dogs, and by the resin which was not given by inhalation and which was less active. The outstanding visceral effect was depletion of lymphoid organs, with testicular degeneration and adrenal abnormality occasionally and, at toxic levels, damage to lungs, liver and kidneys.

DGE was extremely damaging to skin and subcutaneous tissues, producing ecchymoses and coagulative necrosis on contact. Oedema, abscess formation and sloughing followed intramuscular injection in dogs. Corneal opacity followed repeated skin application of 125 mgm. per kgm. to rats, and inhalation by rabbits of 24 p.p.m. DGE caused leucopenia, altered the polymorphonuclear/mononuclear ratio, depressed the marrow and altered the myeloid/erythroid ratio in the 3 species. Repeated exposure of rats to 3 p.p.m. was sufficient to cause such changes, and also eosinophilia and monocytosis and morphological changes. The lowest single dose to produce such effects was 12·5 mgm. per kgm. intravenously to dogs.

DGE should be regarded as a hazardous compound and all contact should be avoided. Changes may be reversible if assessed by laboratory examination before clinical abnormalities occur. This holds also for TGP and epoxy resin A. *M. Patricia Fitzsimons*

GUZMAN, R. J., LOQUVAM, G. S., KODAMA, J. K. & HINE, C. H. **Myocarditis produced by Allylamines. Experimental.** *Arch. Environment. Health.* Chicago. 1961, Jan., v. 2, No. 1, 62–73. [17 refs.]

Rats, rabbits, monkeys or dogs were used in numerous experiments, mainly exposure to various concentrations of vapour, to assess the effects of allylamines on the heart pathology and also on blood, blood pressure, transaminase levels and the electrocardiogram. Myocardial lesions—affecting first the blood vessels and later the muscle—were produced after inhalation of monoallylamine (M), diallylamine (D), triallylamine (T) and bis (2-ethylhexyl) allylamine, but not by *n*-propylamine or diethylenetriamine. Other blood vessels were not affected, and the lesions were different from those produced by sodium fluoroacetate or emetine.

There was individual, species and route variation. For example with M, single or repeated exposure to vapour produced lesions in rats but not equivalent doses by injection, wheras injection produced a lesion in a dog but inhalation did not. Repeated exposure for 7-hour periods to 20–40 p.p.m. caused lesions in rats, but not 4-hour periods at 40 p.p.m. Cardiotoxic effects were potentiated by administration of DOCA and phosphate or of cortisone and phosphate. A similar experiment with allyl alcohol resulted in hepatic and renal damage on potentiation.

The significance of blood pressure changes is discussed: injection of M or D produced temporary hypotension in rats, but inhalation did not. There was some correlation of ECG tracings with the presence of lesions. Transaminase level increase may have been associated with erythrocyte fragility.

M gives warning by its irritant properties, but this will not help with D and particularly T, the last producing lesions at low concentrations without other symptoms of toxicity. It is recommended that the working environment should be monitored and that concentrations of M should not exceed 5 p.p.m. and of

D and T 20 p.p.m. [Figures referred to in the text are not produced.]

[See also this *Bulletin*, 1961, v. 36, p. 339.]

M. Patricia Fitzsimons

STEPHENSON, R. W. & FOSDICK, L. B. **Hazards in the Use of Isopolyesters as Maintenance Coatings.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 522–5, 1 fig.

Precautions are necessary against fire, skin and eye irritation from styrene, skin absorption of dimethylanaline and inhalation of both. Unsaturated polyesters based on isophthalic acid were developed as flexible resins for patching and coating compounds and as rigid resins for laminate construction. Mixing requires good ventilation and the cure " promoters ", cobalt naphthenate or dimethylaniline, should be added and mixed before the cure catalysts, methylethylketone peroxide or benzoyl peroxide. Measures to prevent spontaneous combustion are necessary in storing plastic raw materials, and wiping cloths should be placed in metal covered containers with removable plastic linings which should be promptly removed as should excess uncured plastic constituents. Contact of the oxidizing agents and plastic with combustible material should be avoided. When pouring, styrene containers should have metal contact and sources of ignition, *e.g.*, friction, prevented. Electrical grounding of the spray gun to the resin container and the metal surface being coated is necessary. Splashes of dimethylaniline, a nervous system depressant, should be removed. In laminate construction the application crew wear full protective clothing; otherwise neoprene aprons, polyethylene gloves, goggles or face shields or sometimes respirators.

The MAC of styrene is 100 p.p.m. In a large room 200–700 p.p.m. were recorded during operations. A canister styrene mask can be used if O_2 is above 16% and styrene less than 20,000 p.p.m. (2%), but over this an air-supply mask is necessary. While its irritating properties prevent inhalation, unless the victim is trapped, styrene may cause nausea, vomiting, anorexia and weakness, and it may be detected in the breath for some hours. Animals die from lung irritation or central nervous system depression. During polymerization the temperature rises and styrene combines with the resin to form the final plastic product.

M. Patricia Fitzsimons

KODAMA, J. K., GUZMAN, R. J., DUNLAP, M. K., LOQUVAM, G. S., LIMA, R. & HINE, C. H. **Some Effects of Epoxy Compounds on the Blood.** *Arch. Environment. Health.* Chicago. 1961, Jan., v. 2, No. 1, 50–61. [25 refs.]

Injury to blood formation was especially looked for in investigating 13 epoxy compounds since, when biologically active, they would perhaps produce effects similar to those of ionizing radiation, as do other cytotoxic alkylating agents. Rats were injected intramuscularly on 3 days with a dose to produce toxic but not fatal effects, and in some cases this procedure was repeated after 4 days. Controls were injected with the vehicle, propylene glycol and positive controls with single doses of cytotoxic agents, 0·5 or 5 mgm. per kgm. mechlorethamine HCl or 10 mgm. per kgm. busulfan. Serial white cell and haemoglobin examinations were made and erythrocyte counts if anaemia developed. The animals were killed on the 12th day for marrow counts and histological examinations. Methods for standardizing estimations are described.

The compounds are numbered in order below, with each dose in mgm. per kgm. in brackets.

1. Glycidol (100)
2. *n*-Butyl glycidyl ether (400)
3. Phenyl glycidyl ether (400)
4. Allyl glycidyl ether (400)
5. Glycidyl aldehyde (50)
6. Butadiene dioxide (25)
7. Diglycidyl ether (25)
8. Vinylcyclohexene diepoxide (400)
9. Glycidylphenyl glycidyl ether (200)
10. Epoxy resin B (800)
11. Diglycidylphenyl glycidyl ether (200)
12. Triglycidyl phosphate (25)
13. Epoxy resin A (100 & 200) = glycidyl-O-R-O-glycidyl, where R consists of aliphatic radicals with average molecular weight of 100.

Most were harmful. Anaemia appeared with No. 9, leucopenia with Nos. 6, 7 and 12, and both with 4, 8 and 13. The polymorphonuclear/mononuclear ratio was reduced with 5, 8 and 13. Marrow nucleated cells were reduced with 5, 8, 12 and 13, and the myeloid/erythroid ratio altered with many. Weight loss was prominent and histological findings agreeing with those reported following radiation, radiomimetic chemicals or starvation were most frequent in thymus, spleen and testis. Liver, lung and pancreas also were affected by No. 4, and liver by Nos. 8 and 13. The " radiomimetic " effects were less than those from the positive controls, but should be kept in mind. [See HINE *et al.* p. 538.] [See also this *Bulletin*, 1957, v. 32, 162; 1958, v. 33, 769.]

M. Patricia Fitzsimons

ZIELHUIS, R. L. **Systemic Toxicity from Exposure to Epoxy Resins, Hardeners, and Styrene.** *J. Occup. Med.* Chicago. 1961, Jan., v. 3, No. 1, 25–9. [10 refs.]

The serum electrophoretic protein pattern showed a difference when the subjects of this investigation were subdivided into groups of fit and unfit men. The unfit had lower albumin and higher beta and alpha globulin percentages than the fit whose data agreed well with figures reported for normal men. A relationship, not necessarily causal, is suggested with allergic eczema, which presented the main problem.

The subjects were workers in an aircraft factory in the Netherlands. In department A the inner surface of large hollow objects is impregnated by hand brushing with resins and polyamine mixture, mainly triethylenetetramine. The curing agent may also contain small quantities of allyl glycidyl ether, cresyl glycidyl ether,

cyclohexanol, decalin and glycols. Other men are occupied in moulding and grinding. In department B small airplane parts are made from polyester fibre-glass material. The volatile products are styrene, mixed with cobalt naphthenate, dioctylphthalate, and petroleum naphtha or with a resin; methylethylketonhydroperoxide in dimethylphthalate; and other curing agents. Quantities handled are mentioned but no atmospheric concentrations.

Clinical examinations, liver function tests and several blood, urine and enzyme examinations were made in 50 men; 21 were examined 2–4 times at 6-month intervals. All were exposed to styrene or triethylenetetramine, and some to both. Men with about 1 year's exposure in department A had relative lymphopenia; this was not related to eczema, drowsiness or high exposure. Haemoglobin values were decreased, but not significantly. Men in department B after 15 months' exposure had an increase in positive urobilin tests, significant only if a trace and clearly positive reaction were weighted equally. No clear evidence of general toxicity was established and the investigation is being continued. [See also pp. 538, 539.]

M. Patricia Fitzsimons

Dolgov, A. P. & Solovieva, L. V. **[Skin Diseases caused by Epoxy Resins and Compounds prepared on its Basis]** *Gigiena Truda i Professional'nye Zabolevaniya.* Moscow. 1961, v. 5, No. 1, 23–7. [In Russian.] English summary.

Work with many polymers can provoke skin disease; the data of the dermatological section of the Institute of Industrial Hygiene and Occupational Diseases of the Academy of Medicine of the U.S.S.R. revealed that polymers were responsible for 20% of all industrial dermatitis.

An investigation is described into the causation of dermatitis in epoxy resin workers to determine the importance of epoxy resins, hardeners, plasticizers and fillers. 48 patients having contact with epoxy resins were investigated. In the majority the skin disease was localized to the exposed parts; neck, face and upper extremities—this is interpreted as indicating that the direct action of the products is significant in the cause of the disease, particularly as resins with a sticky consistency can remain for a long time on the skin. The frequent complaint of irritation of the unexposed parts of the body which were clinically normal is interpreted as absorption by the clothes of components of the epoxy resins although atmospheric sampling did not detect their presence.

The patients were studied by means of drop tests [the technique is not described] which indicated an increased sensitivity. In 18 patients a reaction "equal with the clinical manifestation" developed on application of resins ED-5, ED-6, ED-14, ED-40 and ED-41 (the epoxy number is determined by the ratio of epichlorhydrin and diphenylolpropane. Thus resin ED-5 contains 20–22% of epoxy group; ED-6, 14–18%; ED-13, 8–10%; ED-15, 5–7%; ED-37, 11–16% [*sic*]. Resin ED-5 is very thin but ED-15 and 13 are hard and brittle). These persons had worked only with one resin ED-5 or ED-6, ED-40, etc. In 12 persons, irrespective of the sort of resin with which they had contact, a reaction developed not to all resins but only to ED-5, ED-6, ED-13, ED-40 [this part of the paper is not very clear, it would seem that while all the subjects tested had developed skin reactions while working with epoxy resins, the "drop test" may have included others such as the urea formaldehyde and phenolformaldehyde resins]. It is inferred that epoxy resins are sensitizers irrespective of the epoxy number.

Study of the irritant properties of the components of epoxy resins revealed that reactions to epichlorhydrin were less marked and less common.

Plasticizers (polyethers dibutylphthalate, tricresylphosphate, triphenylphosphate, etc.), and fillers (silica, cement, glass wool and asbestos fibre), are not as a rule responsible for skin diseases when used with epoxy resins.

With regard to hardeners—maleic anhydride, polyethylenepolyamine, hexamethylenediamine act as primary and secondary irritants; the sensitizing action was not strongly marked.

The paper concludes with a review of prophylactic measures, such as avoidance of hand contact, good general hygiene and ventilation and the use of acetone for removing any resin from the hands, followed by washing in soap and warm water. *W. R. Lee*

Birmingham, D. J., Key, M. M., Tubich, G. E. & Perone, V. B. **Phototoxic Bullae among Celery Harvesters.** *Arch. Dermat.* 1961, Jan., v. 83, No. 1, 73–85, 11 figs. [28 refs.] Abstract of Discussion 85–7.

This paper was presented and discussed at the 80th Annual Meeting of the American Dermatological Association, Inc., in April, 1960.

The theories concerning the causation of dermatitis in handlers of celery which have been advanced in reports on the condition are (1) allergic hypersensitivity to celery oil, (2) allergic hypersensitivity to certain varieties of celery, and (3) phytophoto dermatitis. A fourth theory held by Michigan farmers was that the dermatitis was due to "pink rot", a fungus disease (*Sclerotinia sclerotiorum*) of celery.

Described in this paper is the careful and interesting investigation carried out in Michigan where celery has been grown commercially since 1856. In a section of the paper on field studies there is an account of the cutting and handling of celery with a description and photographs of the dermatitis observed in the workers. In a random sample of 302 celery workers 163 displayed various stages of vesicular and bulbous dermatitis. The incidence of dermatitis was (1) much greater in the field workers than in those who handled the celery in sheds, (2) greater in farms where celery was cut by hand than in those with mechanized cutting, and (3) small among Mexican and Negro workers. Some patch tests were carried out on 25 field workers to "ascertain the role of allergic sensitivity versus that of photoreactivity to normal or pink-rot celery". The results indicated that eczematous contact allergy to celery oil was not the common cause of the eruptions but that a photoreactive material was present in pink rot celery.

Laboratory studies were carried out to study the cutaneous lesions on human and animal skin after application of normal and diseased celery along with natural and artificial light stimuli and to try to identify the photoreactive chemical " through characterization of its absorption spectrum ". The results are described in detail.

Among the conclusions are (1) pink-rot celery contains a photoreactive material which can produce the skin lesions on irradiation by sunlight or a carbon arc lamp emitting wavelengths between 3,200 Å and 3,700 Å. Some indications of the nature of chemical substances present in pink-rot celery were obtained by infra-red and ultra-violet absorption spectrophotometry. Cutaneous reactions could not be produced by normal celery. The prevention of celery dermatitis by protective clothing and physical and chemical sunscreens is described. *M. E. Delafield*

NEWELL, R. R. **Radiation Hazard in Industry. An Operating Rule for Maximum Possible Doses reasonably assures Satisfactory Protection of Health and Negligible Augmentation of Genetic Mutations.** *J. Amer. Med. Ass.* 1961, Jan. 21, v. 175, No. 3, 227–9, 1 fig.

The International Commission on Radiological Protection (ICRP), for 1958 recommended as the maximum permissible dose (MPD) for occupational exposure (N–18)5 rems for gonads, blood-forming organs and lenses of the eye. N is the age of the employee who must be at least 18. Emergency exposure is permitted up to 12 rems but if the accumulation exceeds the formula, the excess shall be made up, as the author puts it!

A further report by the U.S. National Committee of Radiation Protection (NCRP) in the National Bureau of Standards Handbook 69 (1959) tabulates the maximum permissible body burden for nearly every radioactive nuclide, according to the organ that may be critical. We are, says the author, to gain the impression that they permit injury to go just so far and no farther. He is sure that even within the NCRP the MPD has come to be taken as a measure of radiation injury— " the amount of injury that our conscience can condone ". He challenges, and many will think quite rightly, the claim that the MPD is a statement of a degree of injury; it is simply an operating rule.

This rather remarkable adjustment of the dose of ionizing radiation to what can be carried out in practice dates back to the first attempt of this kind made by the British Committee on X-ray and Radium Protection nearly 40 years ago. Successive years have reduced their first attempts at setting a safety limit to what one can tolerate indefinitely. Since those early days the sinister threat of undesirable genetic changes induced by radiation has inevitably led to more and more effort to reduce unwanted radiation to an absolute minimum. Keeping to the rules laid down in recent years assures a negligible augmentation of genetic mutations.

S. Russ

MELVILLE, G. S., Jr. & RIESS, R. W. **Rare-Earth Nitrate and Oxide. Effects on Irradiated and Nonirradiated Rats.** *Arch. Environment. Health.* Chicago. 1961, Feb., v. 2, No. 2, 178–84, 8 figs.

This is an account of experiments arising out of the effects which a reactor accident might have on attending personnel.

The sort of accident envisaged is one in which fission products are released into the atmosphere and any personnel present would be liable to damage by ingestion or inhalation. The rare earth fission products would probably be oxides and nitrates. The primary components are lanthanum, cerium, neodymium, praeseodymium and samarium. In the experiments under review rats were injected either subcutaneously or intraperitoneally and were then given whole body gamma rays from cobalt. Weight for weight the rare earth nitrate in peanut oil was the most fatal to the irradiated rats, though without harmful effects upon the controls. Whole body irradiation has long been known to lower animal resistance to infection but we are here dealing with sterile material introduced into the body.

S. Russ

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

MINISTRY OF AGRICULTURE, FISHERIES & FOOD. **Food Standards Committee. Report on Bread and Flour.** pp. v + 70, 1 chart. [32 refs.] 1960. London: H.M. Stationery Office. [4s. 6d.]

The levels of certain nutrients in flour have been subject to regulation since early in 1940, when flour was enriched with synthetic thiamine. In 1942, an extraction rate of 80–90% for National Flour was introduced, making the addition of thiamine unnecessary; calcium was, however, added to counteract the high content of phytic acid. When the milling industry was finally decontrolled in 1953, addition of vitamin B1, nicotinic acid, iron and calcium carbonate to all flour except whole meal was made compulsory. The effects of the disappearance of the National Flour were considered

by a Panel in 1955 which concluded that, despite some definite differences in nutrient content between the National Flour and enriched white flour, the consumption of the latter would not significantly affect health.

Although the consumption of bread has declined since the war, it is still the most important staple food in the United Kingdom. The National Food Survey for 1958 showed that approximately one-quarter of the calories, protein, iron, vitamin B1, nicotinic acid, and calcium in the diet were provided by bread and flour. In view of the importance of these foods, the National Food Standards Committee was asked to consider regulations pertaining to bread and flour. Its report covers such points as the definition of the terms applied to different types of flour, minimum levels of certain nutrients, the means by which standards are to be controlled, the use of additives, and the restriction of claims made by manufacturers regarding the properties of bread and flour.

No statutory limits were laid down for the protein, ash, fibre or moisture content of white flour, because of the many different kinds of grain used in producing English flour. It was recommended that the content of iron, vitamin B1, and nicotinic acid should be maintained at the present levels of 1·65, 0·24 and 1·60 mgm. per 100 gm. of flour respectively, added to white flour in the form of a master mix of controlled composition. Calcium should continue to be added in the form of creta praeparata (finely powdered calcium carbonate) at levels of between 235–390 mgm. per 100 gm. of flour. Some flours, for instance self-raising flour, contain considerable quantities of calcium salts other than calcium carbonate. The Committee stated that there was no objection to this, as long as the calcium content was equivalent to that of creta praeparata in plain white flour. It was however recognized that creta praeparata was perhaps not the best substance for calcium enrichment, since it was difficult to disperse it uniformly. Research into the possibilities of using other sources of calcium, and also the general improvement of methods of adding and dispersing the nutrients, were recommended.

The Committee realized that millers could not at present comply consistently with the statutory regulations, but hoped that milling practices would improve so that more uniform production could be achieved. In the meantime the regulations should be enforced as far as possible by compulsory inspections of mills and periodic analyses of flour and the master mix. The enforcement of flour regulations is in the hands of local food and drug authorities. The Committee expressed the view that a central inspectorate would be more efficient; failing this, there should be appropriate co-ordination between local authorities.

The question of bleachers and improvers was referred to a sub-committee whose findings are given in detail in Appendix V of the report. Since the flour used in the United Kingdom is made from a variety of home-grown and imported grains, completely unadulterated flour would not meet the tastes of the consumers, who are used to consistently white flour and a uniform bread texture. Only a limited number of bleachers and improvers, used in limited quantities, should, however, be permitted. Small amounts of enzymes could be added to flour, but emulsifying agents should be used only in pre-mixes for bread-making. Caramel for use in currant and malt loaves was the only permissible colouring matter to be added to any type of flour.

Bread was considered by the Committee under a separate heading. It recognized that a nutrient standard for bread was not practicable because of the impossibility of standardizing baking conditions. Wide variation in water content and heat destruction of nutrients was inevitable, and difficulties in analysing representative samples of bread added to the difficulty of enforcing a standard product. Emphasis was therefore laid on the ingredients other than flour used in bread-making, and a list of permissible ingredients is given.

This section of the report is concerned mainly with claims made by manufacturers about the properties of specific kinds of bread. Frequently these include misleading terms like "slimming" or "high-protein". The Committee emphatically declared that no food could properly be termed "slimming" and that bread called "protein", "starch reduced" or "milk bread" must be of appropriate and well-defined composition.

For the adequate study of the Committee's conclusions and recommendations, the report itself must be read, and especially the appendices which give in detail the findings of advisory sub-committees. These include, in addition to data on bread and flour ingredients and additives, some interesting information on national food consumption and health during 1950–60.

Ruth Schwartz

SEMPLE, A. B., GRAHAM, A. J. & DUTTON, E. M. **A Review of the Sampling of Imported Desiccated Coconut.** *Med. Officer.* 1961, Feb. 3, v. 105, No. 5, 59–60.

The report covers a 10-month period in which 380/6,567 samples of desiccated coconut sampled in the Port of Liverpool were positive for salmonellae of 33 different serotypes including *Salmonella paratyphi B* (32), *Salm. typhi-murium* (13) and Salm. Thompson (2) as well as many others classified as "undesignated" by the authors [most of these serotypes are known to be associated with human salmonellosis, *e.g.* Salm. Waycross, Salm. Perth, Salm. Hvittingfoss, Salm. Stanley, Salm. Oslo, Salm. San Juan, Salm. Simsbury, Salm. Rubislaw, Salm. Bareilly, Salm. Senftenberg, Salm. Litchfield, Salm. Newport, Salm. Nchanga, Salm. Chester, Salm. Butantan, Salm. Virchow, Salm. Welikada, Salm. Onderstepoort, Salm. Muenster, Salm. Poona, Salm. Weltevreden, *Salm. javiana* and *Salm. infantis*].

Month by month from February to October 1960 the percentage of contaminated samples was 7·9, 6·6, 2·1, 1·8, 5·4, 7·1, 7, 6, and 8·4.

Random sampling was soon replaced by the examination of 5% samples from each "lot" or "code" from every consignment; followed by 10% sampling if any were positive. At first when any of the 10% samples were positive the code was condemned, if negative the individual bags only from the 5% samples were condemned; now the 10% sampling is abandoned if 5%

samples contain " non-designated " salmonellae only, and the whole consignment is released. It was realized that this method of sampling was inadequate when 1 only of 51 samples from a single bag was found to be positive for *Salm. paratyphi B.*

It is emphasized that a single sample is not representative of a whole bag and that therefore many bags are released which if fully sampled would show evidence of serious contamination.

It is suggested that only consignments of desiccated coconut subjected to repeated sampling should be released and that adequate standards of hygiene should be enforced in Ceylon. [Methods of treatment by steam, fumigation and irradiation are being investigated.]

Betty C. Hobbs

SMITH, H. W. **The Effect of feeding Pigs on Food naturally contaminated with Salmonellae.** *J. Hygiene.* 1960, Dec., v. 58, No. 4, 381–9. [14 refs.]

24 pigs aged 8 weeks, from 4 litters belonging to a self-contained herd fed with mixed foodstuffs, were housed in special accommodation. Mesenteric glands from 40 pigs belonging to the same herd had been examined for salmonellae over a period of 3 months with negative results.

20 of the experimental pigs were fed on a diet which included Angola fishmeal (10%) and Pakistan bonemeal (2%) containing 2 (50 per 100 gm.) and 16 (700 per 100 gm.) salmonella serotypes respectively. Both supplements were omitted from the diet of the 4 control pigs. Faeces samples were examined before and at intervals of 2–6 days after the experiment commenced. The pigs were killed at varying times and their organs examined for salmonellae. None of the pigs showed any signs of ill-health and no pathological lesions were found. 21 salmonella serotypes, including all those found in the supplements, were found in small numbers in the mesenteric lymph nodes of some pigs, but not in any other organ or muscular tissue. The longer the pigs were fed on the contaminated food the more likely were the mesenteric lymph nodes to be infected. The faeces were also positive from time to time although not permanently.

6 of the pigs were fed on a salmonella-free diet for a short time after the 50-day period of the experiment. Their faeces were negative and salmonellae were found in mesenteric lymph nodes from 1 of 6 only. Salmonellae were not found in the control pigs killed after 50 days.

It is considered that the main danger of feeding salmonella-contaminated food to pigs lies in the risk of meat becoming contaminated by alimentary contents at slaughter, so that man is infected. It is suggested that the importation of contaminated supplements should be prohibited, or that they should be treated, or that they should be withdrawn before slaughter.

[See also this *Bulletin,* 1959, v. 34, 670.]

Betty C. Hobbs

BERGNER-RABINOWITZ, S. **Evaluation of the Sanitary Purity of Milk and Milk Products by a Plate Method.** *Bull. Res. Counc. of Israel.* 1960, Nov., v. 8E, No. 4, 135–40. [14 refs.]

Bacteriological standards for milk and milk products were recently established in Israel (Kowetz Hatakanoth, 1958, Sept., 825, p. 1939, *Rules and Regulations*). From September 1955 to December 1957, the most probable number (MPN) of coliform bacilli was determined for 1,980 samples of pasteurized milk in lactose broth; the results varied from less than 1 to 240 per ml. There was no seasonal variation and the milk improved during 1957 so that 78% of the samples tested during the last 6 months of 1957 showed not more than 2–3 coliform bacilli per ml.

400 samples of both fruit and milk ice-cream were examined also. The coliform MPN, for fruit ice-cream, varied from less than 1 to 240 per ml., but for milk ice-cream 50% of samples contained more than 700 coliforms per ml.

A standard is proposed whereby the coliform count is not to exceed 1 per ml. in 3 out of 4 examinations. It is thought that the coliform count gives a better index of contamination than the total bacterial count.

Solid media appeared to give more accurate although lower results than liquid media. A MacConkey pour plate with a covering layer of agar was used. After 20–24 hours' incubation at 35° C. all red colonies of 0·5 mm. and over were counted, 92% colonies were found to be Gram-negative bacilli able to ferment lactose.

The test was simple and results could be obtained after 18–24 hours' incubation; it is recommended for routine examination of milk and milk products throughout Israel.

Betty C. Hobbs

SMITH, J. **Reviews of the Progress of Dairy Science. Section F. Milk-Borne Disease.** *J. Dairy Res.* 1961, Feb., v. 28, No. 1, 87–107. [100 refs.]

FOOD POISONING

GHOSH, R. N., GHOSE, D. N., LAHIRI, M. N. & BHATTACHARJEE, L. M. **Bacteriological Investigation of an Outbreak of Food Poisoning due to Salmonella Newport in Calcutta.** *Indian J. Pub. Health.* 1960, Apr., v. 4, No. 2, 61–7. [11 refs.]

In July 1958 cases of food poisoning with symptoms of diarrhoea, vomiting, fever, headache, body ache and abdominal pain, occurred in a hostel; the duration of illness was 3 days. Salmonella newport was isolated from 12 of 16 stool samples from patients and from 1 of 15 stools from kitchen staff. Samples of blood from 9 patients each agglutinated the salmonella strains isolated from each stool.

Left-over food, including custard powder, cream,

curry, and *sag-dal,* and also washings from empty pineapple cans were examined with negative results.

On epidemiological grounds the custard powder, used to make a particular food eaten by all those affected and not by others, was thought to be the vehicle of infection.

Salm. newport has not previously been known to cause food poisoning in India. *Betty C. Hobbs*

FEE, W. M. **An Unusual Vehicle of Infection.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1961, Jan., v. 19, No. 1, 10–12.

8 persons from at least 4 different families were taken ill 2–2½ hours after eating gammon purchased from the same shop in warm weather. Coagulase-positive staphylococci of the same phage type (food poisoning group) were isolated from samples of gammon obtained from one home, from a roll of gammon in the shop, and from debris on the blade of the bacon slicer; the gammon in stock was negative. The phage types of staphylococci from the nares of the 4 members of the shop staff were different from each other and from that of the gammon strains. Faeces and throat swabs were negative, and faeces from patients were negative also.

The bacon slicer was placed on the counter in immediate proximity to customers and there was no routine procedure for dismantling and cleaning the machine. There was a wash-hand basin with running cold but no hot water, no nail brush or notice recommending handwashing. The refrigerator was without a thermometer and its temperature was atmospheric. The proprietor had recently suffered from a cold and dermatitis, and one assistant had dirty finger nails. In all, Regulations 6a, 9, 13(1), 20(4), 22(2), and 22(3) of the Food Hygiene (Scotland) Regulations, 1959, were contravened.

A family doctor was commended for rapid diagnosis, identification of suspected food and immediate notification by telephone to the Public Health Department.

Betty C. Hobbs

HUISMAN, J., DOEGLAS, H. M. G., BUREMA, L. & HERMANS, E. H. Epidemiologische opsporing en klinisch beeld van de ziekte, ontstaan na het gebruik van Planta-margarine. [**Epidemiological Detection and Clinical Picture of the Disease arising after Consumption of "Planta" Margarine**] *Nederl. Tijdschr. v. Geneesk.* 1960, Sept. 17, v. 104, No. 38, 1828–33, 5 figs. English summary.

The authors describe an outbreak throughout the Netherlands in August, 1960, of a febrile illness accompanied by skin manifestations. This illness was apparently related to the consumption of a product known as New Planta margarine. 25% of the people known to have eaten this food developed symptoms and 75% of these patients were women.

The clinical manifestations included urticaria and exudative erythema multiforme. The authors describe, with 5 illustrations, the course of the illness in detail. Symptoms occurred 1 hour to 1 day after consumption of the margarine. The rash appeared first on the face and hands and then spread to the arms, shoulders, trunk and legs. The primary efflorescences were ½–1 cm. erythematous macules which become urticarial after some time. In some patients the lesions were violet in colour. When the rash was generalized the cheeks and lips became oedematous and lesions round the mouth were associated with oedematous gums and blood blisters in the palatal mucosa.

Pyrexia occurred only in those patients whose rash was generalized and the most serious manifestations accompanied a pyrexia of 41° C. where circulatory collapse occurred. One patient had oliguria. Several patients complained of headache and difficulty in swallowing.

Laboratory findings include leucocytosis (11,000–30,000 per cmm.), with a shift to the left on the first day, and eosinophilia of 5–30%. The Rumpel-Leede test was positive. The urine was normal. In histological section there was inter- and intra-cellular oedema, and perivascular infiltration with histiocytes, lymphocytes, and changed eosinophils. In different sections many neutrophils and eosinophils were found. There was no evidence for the cause of the illness being bacterial or viral. Investigations for allergic reactions by doing patch tests on 10 patients were all negative.

The course of the illness was generally benign but the most seriously ill patients were treated with corticosteroids.

The authors then try to correlate the outbreak with the German Bläschenkrankheit (see above) and think that there might be some connexion. *Anne Tothill*

HERMANS, E. H. Enkele aspecten van de margarineziekte. [**Some Aspects of "Margarine Disease"**] *Nederl. Tijdschr. v. Geneesk.* 1960, Oct. 29, v. 104, No. 44, 2157–63. [25 refs.] English summary.

An outbreak of a febrile illness in the Netherlands in 1960 is clinically identical with the "*Bläschenkrankheit*" which occurred in Germany in 1958 [this *Bulletin,* 1960, v. 35, 509]. Both outbreaks followed the appearance on the market of a new type of margarine to which an emulsifier ME 18 had been added. The author describes the course of the German epidemic of 1958.

Several hypotheses as to the aetiology of the disease are discussed. The likelihood of the disease being infectious erythema is improbable because whereas this disease affects mainly children and young people, margarine sickness was almost confined to adult women. The rash in infectious erythema is not found circumorally, as is the case in margarine sickness. The author mentions several other features of divergence in the clinical picture. Exudative erythema multiforme is discarded as a possibility as it affects mainly children. The lesions of margarine sickness are never seen in the typical cockade formation of exudative erythema multiforme. Although the probability of the disease being caused by a virus was investigated and several types of ECHO virus (4, 5, 9, 10 and 12) were isolated, they were not pathogenic.

The author then outlines several puzzling aspects of the disease—of 1,160 patients 73·2% were women, the disease disappeared in spite of continued use of the

emulsifier, large quantities of emulsifier had no effect whereas small amounts gave rise to symptoms, and a reintroduction of the emulsifier in Berlin in 1959 did not give rise to a fresh outbreak.

The author suggests that the emulsifier itself is not the primary cause, but that biochemical changes which it undergoes in the margarine and in the body give rise to products which may be responsible for the clinical manifestations. *Anne Tothill*

JANSEN, L. H., YOUNG, E. & HEIJMANS, H. H. Enkele onderzoekingen naar aanleiding van de zg. Plantaziekte. **[Investigations in Connexion with the So-Called Planta Disease]** *Nederl. Tijdschr. v. Geneesk.* 1960, Oct. 29, v. 104, No. 44, 2163–9, 4 figs. English summary (8 lines).

An outbreak in the Netherlands in 1960 of a febrile illness with skin manifestations is thought to have been due to an emulsifier which was included in Planta margarine. The emulsifier is a triglyceride with one cyclic acid residue. The compound is at present being investigated for antigenic properties.

The authors conducted skin tests on 30 persons, 8 of whom had an allergic constitution and none of whom had had symptoms of Planta disease. Scratch tests with emulsifier in a dilution of 1:1000 were negative in all cases but when the compound was used in a dilution of 1:100, 2 patients had a borderline positive reaction after 20 minutes. Scratch tests with cyclic acid in a concentration of 1:1000 were weakly positive in only 1 case (the 1:100 concentration was negative in the same person), and there were 4 borderline positive reactions after 20 minutes. Intradermal tests with the emulsifier and cyclic acid in a concentration of 1:10,000 were negative in 9 persons.

Skin tests with 50% emulsifier on 13 patients actually suffering from Planta disease were negative but the cyclic acid test on 8 patients was weakly positive in 1 case. Scratch tests in a concentration of 1:1000 with and without cyclic acid were negative, but in a concentration of 1:100 with cyclic acid 2 patients gave doubtful positive results in 20 minutes. Intradermal tests were all negative when cyclic acid was not added but weakly positive in 1 case when cyclic acid was present.

In a group of 14 patients who had developed the disease 1 month previously and had recovered from it scratch tests were all negative.

In contrast to all the preceding negative results the Prausnitz-Küstner test carried out on 13 normal persons with the sera from patients, the emulsifier and the cyclic acid gave negative results in all cases but 2 test subjects showed delayed sensitivity.

The results of all the investigations thus show that no difference could be detected in skin reactions between subjects who had and had not had Planta disease, and no conclusion can be drawn as to the aetiology of the disease. *Anne Tothill*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

SHANON, J. & RAUBITSCHEK, F. **Tinea Faciei simulating Chronic Discoid Lupus Erythematosus.** *Arch. Dermat.* 1960, Aug., v. 82, No. 2, 268–71, 4 figs.

4 cases of tinea faciei are reported in this communication. All occurred in subjects of advanced age (55–65 years), and in all the facial lesion was associated with lesions elsewhere (finger nails, toe nails, lower abdomen).

In 2 of the patients facial and other lesions yielded *Trichophyton rubrum* in culture, while in 1, *T. gypseum* (*T. mentagrophytes*) was recovered, and in the cultures were negative although mycelium was demonstrated by periodic-acid-Schiff staining reaction.

In 1 of the patients (infected by *T. mentagrophytes*) the other involved sites were the left toe nails and the left interdigital clefts; in 1 (infected by *T. rubrum*) the associated lesion was on the lower abdomen; in 1 (infected by *T. rubrum*) the associated lesions were in the nails of the left hand and all the nails of both feet; in the remaining patient, the associated lesion was in a finger nail of the right hand, but, although mycelium could be demonstrated microscopically, no culture could be obtained.

All the patients were markedly sensitive to light and "had developed atrophy, telangiectasia and senile keratoses on exposed areas".

The gross clinical appearances resembling discoid lupus erythematosus were "produced by a superimposition of the inflammatory raised border of the tinea circinata on a skin already atrophic".

It is also the opinion of the authors that the histological findings which resembled those of discoid lupus erythematosus could be explained by the "physiologic aging of the skin aggravated by an actinic factor". *C. J. La Touche*

KATZENELLENBOGEN, I. & SANDBANK, M. **[The Treatment of Tinea Capitis and Dermatomycosis with Griseofulvin. Follow-up of 65 Cases]** *Harefuah.* Jerusalem. 1961, Feb. 15, v. 60, No. 4 [in Hebrew 111–14, 6 figs. English summary 114–15].

The English summary appended to the paper is as follows:—

"This is a report of 65 hospitalized cases with ringworm infection treated with griseofulvia from February 1959 through April 1960. (A preliminary report was published in 'Harefuah' August 1959).

"Types of infection treated included: 19 cases of tinea capitis (including 1 case of favus), 1 case of granuloma trichophyticum, 1 case of sycosis barbae, 32 cases of dermatomycosis, 30 cases of onychomycosis (including patients with infection of both skin and nails).

"Cultures yielded: *T. violaceum* in all but 2 cases of tinea capitis, 1 case with *Achorion Schoenleini*, 1 case with *T. ferrugineum* in a pregnant woman, 25 cases with *T. rubrum* and 5 cases with *T. tonsurans*.

"The patients ranged in age from 15 months to 75 years and the duration of the infection from 1 month to 26 years.

"*Dosage*: While larger doses, 2 gms. daily, were given at first (1959), it was later found that smaller doses —0·5—1·0 gms. daily gave the same good results. Thus in 1959 a total of 84 gms. in 122 days was given in the treatment of tinea capitis in a 10 year old child, while in 1960, 36 gms. in 51 days cured a child of about the same age.

"*Clinical response*: Itching of glabrous skin lesions in all patients subsided after 2—6 days. All glabrous skin lesions faded in a week. There was a more rapid response in the large free areas than in the skin folds, palms or soles in which it took 2—4 weeks before signs of improvement became visible.

"*Side effects*: Undesirable effects produced by griseofulvin were negligible. Headaches, discomfort in the epigastric region and irritability were experienced in a few cases at the beginning of treatment but did not necessitate interruption. In 1 woman with acrosclerosis and favus of the head and nails, high temperature and a rash followed ingestion of griseofulvin, and again when griseofulvin was given a second time. However, successful and uneventful treatment was achieved with the addition of prednisone.

"In 1 case with a severe *T. rubrum* infection lasting over 26 years and covering practically the whole body, dramatic response was seen after a week of griseofulvin treatment. However, new lesions reappeared each time griseofulvin was discontinued. A maintenance dose of 500 mgs. was effective in keeping the patient symptom free.

"In onychomycosis best results were achieved in cases infected with *T. rubrum*. 3·5—4·5 months of continuous treatment was the minimum time required to obtain normal fingernails, while toenails required longer treatment."

BERLIN, C., TAJER, A. & YAIR, C. **[Treatment of Tinea Capitis and Selected Cases of Dermato- and Onychomycosis with Griseofulvin]** *Harefuah.* Jerusalem. 1961, Feb. 15, v. 60, No. 4 [in Hebrew 115–16. English summary 116].

The English summary appended to the paper is as follows:—

"Our experience with oral treatment of tinea capitis, tinea unguium and tinea corporis with griseofulvin is reviewed. Among 35 cases of ringworm of the scalp due to *Trichophyton violaceum* there were 2 mothers. The daily dose for children was 25 mg. per kilo body weight and for the adults 1 gm., with gradual reduction of the dose after the first negative microscopic examination. Tincture of iodine 5% was applied topically to the affected lesions. Complete cure was achieved after an average of 44 days of treatment. No recurrences occurred during a follow-up of 1—4 months.

"In 9 cases of onychomycosis of the fingers marked improvement and sometimes cure was achieved with 1 gm. of the drug given for 6 months.

"In 16 cases of recalcitrant infection of the glabrous skin due mostly to *Trichophyton rubrum* 1—1·5 gm. of griseofulvin a day for several weeks caused apparent cure. Cessation of treatment or even reduction of the dose usually resulted in relapses.

"Tolerance was good in all children. Several adults complained temporarily of nervousness or headaches sometimes associated with dizziness. These side-effects disappeared after the dose was reduced."

YAIR, C. **[The Treatment of Tinea Capitis with Potassium Iodide]** *Harefuah.* Jerusalem. 1961, Feb. 15, v. 60, No. 4 [in Hebrew 117. English summary 117].

The English summary appended to the paper is as follows:—

"35 cases of tinea capitis were treated with 2·5% potassium iodide solution in a dose of 0·5—1·5 Gm. daily. The age of the patients ranged from 2—5 years. The treatment was given for periods of 1—6 months. In most cases treatment was stopped because of lack of cooperation from the children and their families.

"In a few cases slight side-effects were seen. Complete cure was achieved in only 7 cases who had been under treatment for some 3 months."

DONALD, F. G. **Recent Advances in the Treatment of Superficial Fungous Diseases: the Use of Antifungal Antibiotics.** *Med. J. Australia.* 1960, May 14, v. 1, No. 20, 762–4. [13 refs.]

This report is concerned chiefly with the results of oral griseofulvin treatment of patients suffering from tinea capitis due to *Microsporum canis* and *Trichophyton tonsurans*.

In the case of *M. canis* infection, 1 gm. per day for 1 week was administered to children over 3 years of age; 500 mgm. daily for 1 week to children under 12 months old, and 750 mgm. daily to those whose ages lay between 1 year and 3 years. After the first week a daily dose of 250 mgm. was administered to all the children for a further period of 3 weeks.

Weekly shaving and twice daily washings with soap and water followed by the application of a keratolytic ointment containing 3% salicylic acid comprised the supplementary therapy to the scalp in order to rid it of

superficially adherent infective material. In cases where there was a pustular reaction an antibacterial ointment was used instead of the ointment containing salicylic acid.

This course of treatment resulted in the cure of 28 children out of a total of 32 who were treated.

61 aboriginal children suffering from tinea capitis of endothrix type were given oral griseofulvin in a dosage of 1 gm. daily for 25 days, supplemented by the topical treatment outlined above. Response to this treatment was most satisfactory. *C. J. La Touche*

ZIPRKOWSKI, L., KRAKOWSKI, A. & MILLET-SCHEWACH, M. **[Dermatitis Medicamentosa due to Griseofulvin]** *Harefuah.* Jerusalem. 1961, Feb. 15, v. 60, No. 4 [in Hebrew 118. English summary 118–19].

The English summary appended to the paper is as follows:—

"Two cases of drug eruption among 500 patients who received griseofulvin therapy are described.

"In one case griseofulvin was the only drug administered. The eruption disappeared rapidly after withdrawal of the drug and did not reappear when it was readministered. This, in the authors' opinion, does not necessarily rule out the causal relation between the griseofulvin and the eruption, as there may sometimes be a refractory period lasting a short time after the first reaction.

"In the other case, the connection between griseofulvin and the eruption was confirmed when readministration of the drug was followed by a violent reaction approaching shock 1 hour after the taking of one 250 mg. tablet.

"The authors expect that complications due to treatment with griseofulvin are likely to increase in frequency. They therefore recommend its use only in cases with definite indications."

MCDONOUGH, E. S., GEORG, Lucille K., AJELLO, L. & BRINKMAN, Sherry. **Growth of Dimorphic Human Pathogenic Fungi on Media containing Cycloheximide and Chloramphenicol.** *Mycopathologia.* The Hague. 1960, July 30, v. 13, No. 2, 113–20, 2 figs. [10 refs.]

This article contains an account of investigations on the sensitivity of pathogenic fungi in culture to cycloheximide and chloramphenicol, 2 substances now frequently incorporated in culture media used for the purpose of isolating pathogenic fungi from native material.

A number of strains of the following fungi were used for these investigations: *Blastomyces dermatitidis* (24 strains), *Histoplasma capsulatum* (5 strains), *Paracoccidioides brasiliensis* (5 strains) and *Sporotrichum schenckii* (5 strains).

Results showed that, as previously observed [see this *Bulletin,* 1960, v. 35, 981] strains of *B. dermatitidis* were more sensitive in the yeast phase than in the mycelial phase to cycloheximide and chloramphenicol, and that this was also the case with the other fungal pathogens which were thus investigated.

It was also shown that, whereas concentrations of 0·5 mgm. per ml. of cycloheximide and 0·05 mgm. per ml. of chloramphenicol were in most cases suitable concentrations for isolation media incubated at 25° C., some pathogenic fungi were suppressed by these concentrations when the culture media were incubated at 37° C.

In conclusion, the authors recommend that not more than 0·2 mgm. per ml. of chloramphenicol be incorporated in sputum to be cultured subsequently for the pathogenic fungi which are mentioned in this work. *C. J. La Touche*

GARRISON, R. G. **Studies of the Respiratory Activity of *Histoplasma capsulatum*. I. Aspects of the Aerobic Metabolism of the Yeast Phase.** *J. Infect. Dis.* 1961, Jan.–Feb., v. 108, No. 1, 120–24, 3 figs. [17 refs.]

TAKAYAMA, K. **Study on Anti-*Candida* Action of a Strain of *Bacillus subtilis*.** *Kurume Med. J.* 1960, v. 7, No. 1, 56–75, 17 figs.

The origin of this work was an attempt to isolate from the faeces of consumptives a phage which would attack the *Candida* in their sputa. An area of lysis observed proved to be due to the growth of an organism which the author claims to have identified as *Bacillus subtilis.* It forms an inhibitory substance for *Candida albicans,* demonstrable by conventional streaking methods when growing on the surface of a solid medium: the substance is said not to be formed in liquid media, and has no action on most other species of *Candida.* It has been purified to some extent by extraction of cultures on a solid medium with water, adsorption on charcoal and elution with acetone. This extract is non-toxic to mice, and is alleged to have had a therapeutic action when injected intraperitoneally or intramuscularly in single or up to 5 doses, on *Candida albicans* infection produced by the intraperitoneal inoculation of mice. [None of the untreated controls died: the effect was judged by the number of lesions in the peritoneum, liver and spleen. Contrasted organs with few and many lesions are illustrated, as are numerous cultures showing the inhibitory effect, some convincingly and others less so.] *L. P. Garrod*

LOURIA, D. B. & DINEEN, P. **Amphotericin B in Treatment of Disseminated Moniliasis.** *J. Amer. Med. Ass.* 1960, Sept. 17, v. 174, No. 3, 273–9, 3 figs. [18 refs.]

The first case reported in this article was of a woman aged 39 years who was subjected to repeated abdominal operations, not only on account of the presence of disease, but because of adhesions which developed during post-operative periods.

In the course of her surgical treatment it was necessary to establish indwelling catheters, both in the left ureter and in the bladder, and in addition, an indwelling polyethylene catheter in the left cephalic vein for fluid replacement. Chemotherapy during this period included sulfisoxazole [sulphafurazole] and various antibiotics, as well as hydrocortisone.

When, approximately 4 weeks after the initial laparotomy, the patient experienced a sharp rise in temperature, it was found that cultures from all the catheters were positive for *Candida albicans*, as were also the urine, stool and blood cultures.

Amphotericin B therapy was thereupon initiated by intravenous administration in the dosage of 5 mgm. per day. This was then increased rapidly to 50 mgm. per day in 500 ml. of a 5% dextrose solution over a 6-hour period "through small pediatric scalp-vein needles". This treatment was continued until 1,560 mgm. of amphotericin B had been administered.

As a result of this treatment, the patient experienced marked and rapid improvement, and, 6 weeks later, was considered to be "entirely well", and was accordingly discharged.

The second case concerned a man aged 26 who had been subjected to numerous operations since he had undergone an initial ileocolostomy when he was only 3 years old. Before his recent admission to hospital he had received a course of fluids intravenously as well as corticosteroids. On admission he was extremely ill, and when it was found that progressive polypoid degeneration of the distal ileum had set in, an ileosigmoidostomy was carried out. Unfortunately, 3 days after this operation, peritonitis developed, and, accordingly, a laparotomy was performed. Then followed an empyema necessitating thoracotomy.

Chemotherapy during the period of surgical treatment included various antibiotics and steroids, and to ensure adequate drainage of the empyema, a polyethylene catheter was installed.

When this patient's temperature returned to normal all chemotherapy was stopped. However, no sooner was this done than it rose again rapidly, and when blood cultures were made. they were positive for *C. albicans*. Amphotericin B therapy was accordingly instituted, and was met with a remarkably successful response which culminated in the complete recovery of the patient.

The third case was of a woman aged 36 who, after valvotomy, developed monilial endocarditis as revealed by successively positive blood cultures.

Amphotericin B therapy, which was continued for 33 days, was administered to this patient who, as a result, appeared fully to have recovered. However, 2 weeks later she relapsed, and, despite further courses of amphotericin B ultimately succumbed.

As permission for autopsy was refused, no post-mortem findings were available.

The therapeutic value of amphotericin B is thus clearly indicated in these 3 case reports, providing still further evidence of its efficacy in the treatment of systemic mycoses.

C. J. La Touche

GADEBUSCH, H. H. & JOHNSON, J. D. **Specific Degradation of *Cryptococcus neoformans* 3723 Capsular Polysaccharide by a Microbial Enzyme. I. Isolation, Partial Purification, and Properties of the Enzyme.** *Canadian J. Microbiol.* Ottawa. 1961, Feb., v. 7, No. 1, 53–60, 4 figs. [20 refs.]

DE MINJER, A. Pulmonale aspergillosis [**Pulmonary Aspergillosis**] *Nederl. Tijdschr. v. Geneesk.* 1960, Nov. 5, v. 104, No. 45, 2205–10, 8 figs.

The author describes with illustrations the history, clinical features and subsequent course of 5 patients with pulmonary aspergillosis.

The first case is described in detail and concerns an insurance salesman aged 54. 3 months before his death he complained of headaches, lassitude and difficulty in moving his joints. His knee joints were very swollen. He continued work until he developed pain in the chest. He was admitted to hospital 2 months later. On examination he was nervous and restless, complaining of pain on breathing. The chest was dull at the right base and râles were heard. Auricular fibrillation was present. The following day he developed pyrexia of 39·2° C. The white cell count was fairly low with a relative shift to the left. Protein was present in the urine and the sediment contained leucocytes and erythrocytes. The patient was treated with aspirin, heparin and Sinthrone on the basis of a diagnosis of acute rheumatic fever with embolic phenomena. Chloramphenicol was given, as pneumonia was considered possible. Penicillin and streptomycin were then given and the temperature became normal, but the general condition worsened, the left lung became involved and the blood urea rose to 75 mgm. per 100 ml. The temperature rose again and the antibiotics were repeated. Although the blood urea subsequently became normal the urine contained urobilinogen in excess and 135 mgm. per litre of corproporphyrin.

The patient was thought to have lupus erythematosus and received a course of prednisolone. Throughout his illness he received many drugs, including chloroquine, digitalis and different hormone preparations, and several blood transfusions. Despite this vigorous treatment his condition deteriorated and he died. At autopsy there was fibrinous pleurisy and the lungs had patches of necrosis and induration, the latter resembling tuberculous caseation. The lung tissue between the indurated areas was hyperaemic. A diagnosis of aspergillosis due to *Aspergillus fumigatus* was made on the basis of histological and cultural examination. The heart was dilated and fibrinous pericarditis was present. The valves were encrusted with warty thrombi with signs of organization. The tongue was infected with *Candida tropicalis*.

The author describes 4 other cases. A man aged 21 years who had a previous history of bronchial asthma. A lobectomy was performed and the pathological findings are recorded. A man aged 59 years who was diagnosed by means of X-ray and bronchoscopy and 2 others who had previously had extensive courses of antibiotics, corticotrophin and prednisolone.

It is concluded that in the treatment of a primary disease with many and diverse antibiotics and hormones, a secondary mycotic infection with *Aspergillus* or *Candida* may arise.

Anne Tothill

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

TUBERCULOSIS

BRINKMANN, O. Von der Tuberkulosegefährdung in Pathologischen Instituten. [**The Risk of Tuberculosis in Pathological Institutes**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1958, July, v. 8, No. 7, 156–61.

This paper begins with a review of German literature on the risk of tuberculosis to workers in pathology institutes. It goes on to report the results of Brinkmann's enquiry into the subject which he made in 1955 from the heads of 10 institutes in Westphalia.

The period covered was 1950–1954; the consolidated replies are tabulated:

Average annual total					
Doctors	*Post-mortem assistants*	*Laboratory technicians*	*Cleaners (women)*	*Secretaries (women)*	*Cases of TB*
47	18	46	17	11	2 dr. 1950 1 dr. 1952 1 dr. 1953 1 post-mortem asst. 1953

2 cases occurred in 1 institute in 1952 and 1953 respectively, 1 of the other 3 cases occurred in 1 institute and 2 in a third. 6 of the institutes reported no case of tuberculosis, and the return from the remaining institute is shown as doubtful.

There has been no notification of tuberculosis to the industrial disease medical officer in Westphalia from any pathological department in the years 1955–1957.

During the period 1950–1954, 139 persons were employed in the 10 pathological institutes. The incidence rate of tuberculosis in these workers was 1·4% in 1950, nil in 1951, 0·7% in 1952, 1·4% in 1953 and nil in 1954. The institutes in which tuberculosis was contracted in the course of work were in an industrial area which had suffered much war damage and post-mortem examinations were being conducted in makeshift mortuaries where it was not possible to observe hygienic practices.

The fact that a person who contracts tuberculosis is engaged in pathological work is not proof that his disease is an occupational one. Each case must be decided according to its individual circumstances.

H. G. Calwell

SIMMONDS, F. A. H. [M.A., M.D., D.P.H.] **The Protection of the Nurse and other Hospital Workers against Tuberculosis.** 2nd Edition. 95 pp., 11 figs. 1960. London: The Chest and Heart Association, Tavistock House North, Tavistock Square, W.C.1. [12s. 6d.]

The appearance of a second edition of this little book indicates that it has proved of value. It has been completely revised and brought up to date. Since the first edition [this *Bulletin*, 1953, v. 28, 302] the incidence of infectious tuberculosis in Great Britain has decreased; on the other hand the more general in-patient treatment in town as opposed to well-ventilated sanatoria, and the lack of reduction of morbidity in older persons who are often bronchitic has tended to increase the possibilities of infection. Again the existence of resistant bacilli has reduced the general better prognosis from treatment. Certainly the improvement of conditions of work and general use of BCG has enormously reduced the morbidity from tuberculosis among nurses. But in countries where the tuberculous services are not yet developed the possibility of infection of nurses is very high. Thus although the measures advocated in this book are still important here in Great Britain, they are vital in countries where tuberculosis is still rife.

After an excellent short account of tuberculosis the various methods of protection are clearly set out. It is difficult to find points to criticize, but routine X-rays of patients on admission especially men over 40 might be advocated more strongly. The book should be read by all nurses dealing with tuberculosis and should be in the library of every hospital matron and hospital secretary.

F. H. Young

VAN DER REEP, A. F. M. Tuberculose in een plattelands-praktijk. Een medisch-sociografisch onderzoek. [**Tuberculosis in a Country Practice. A Medico-Sociographic Inquiry**] 207 pp., illustrated. [Numerous refs.] English summary. 1959. Alkmaar: N.V. P.O.A.

This thesis for the MD of the University of Nijmegen deals with many aspects of pulmonary and extra-pulmonary disease in a rural practice. 885 families comprising about 4,500 people were investigated and followed-up during the period 1946–1955.

As an introduction to the subject, some of the problems of resistance susceptibility and the place of exogenous and endogenous infection are discussed. Attention is also drawn to the greater importance of epidemiology when the incidence of tuberculosis is on the decline.

The tuberculosis annual morbidity rate in the author's practice was 52·8 per 10,000 with a mortality of 4·1 per 10,000. At the end of the investigation period 400 persons had had or were on treatment for tuberculosis. The incidence was more in females than in males.

The overall tuberculin index (Mantoux text, 5 TU

per 0·1 ml.) was 40%, maxmium conversion being at age 15–34 years (especially 20–24), with the result that the author advises BCG at 10–14 years. The Mérieux test (neotuberculin-albumin free, percutaneous) was found to be fairly reliable, the Mantoux being used as the standard in its assessment.

Families with a history of tuberculosis gave a higher tuberculin index and a greater local skin reaction than families with no such history. There was a similar correlation with post-primary tuberculosis in persons under 22 years old. 27·3% gave no family history of tuberculosis and in 41% there was no known source of infection. The author feels that the disease by keeping the family together, influences family size and not necessarily the reverse. Attention is also drawn to the apparent susceptibility of the 9th and younger children.

There are numerous other interesting observations. 20% of patients were married at the time of diagnosis, 25·3% of family contacts had or had had tuberculosis; home appeared the greatest source of infection; low intelligence appeared to be associated. 21·2% were not fully fit for work, and only 49 out of 253 patients had to change their occupations; as reported by other authors, there was a high incidence among nuns. The lowest incidence was in agricultural occupations. [As the distribution of cases was a little unusual more detail might have added materially to the value of the occupational analysis.] Social analysis showed that only 5 patients suffered a fall in social standing, and 23 actually improved their position in the community. Social and political participation of those under study did not appear to be influenced by the development of tuberculosis. Nutrition showed no correlation with the incidence of the disease.

Diagnosis and primary presenting symptoms are analysed, treatment is discussed and a 5-year follow-up period advised.

Population screening is discussed and it is suggested that this should be directed to special groups, and guided by tuberculin testing.

This is a most interesting epidemiological investigation which not only adds valuable support to many of the current ideas in tuberculosis, but also presents some thought-provoking facts which do not quite fit into the usually accepted pattern. *Kurt Schwarz*

Monaco, A., Cipolla, L. & Sani, A. Rilievi sull'andamento dell'epidemilogia tubercolare in Sardegna con particolare riguardo alla composizione della popolazione ricoverata presso l'ospedale sanatoriale "R. Binaghi" di Cagliari. **[Epidemiological Trends of Tuberculosis in Sardinia with Particular Reference to the Patients of the Hospital-Sanatorium "R. Binaghi" of Cagliari]** *Lotta c. la Tubercolosi.* 1960, Sept., v. 30, No. 9, 785–800.

For many years the tuberculosis death-rate in Sardinia had been the highest in Italy: it is now well below the national average. The incidence of the disease has not shown the same downward trend in recent years. Some 20,000–30,000 new patients are now annually examined in the tuberculosis dispensaries of Cagliari Province, where 1,169 cases of tuberculosis (all forms) were diagnosed in 1949 and 1,476 in 1958; 1,168 of the latter were pulmonary disease.

In the whole island of Sardinia, before the First World War, the average incidence of tuberculosis was some 20,000 cases. In the last 5 years, this annual average is down to some 6,142 cases. With the introduction of specific antibiotic drugs the incidence rate has been reduced by about two-thirds, to 4·4 per 1,000. The rate of new cases is 1·7 per 1,000, but this has shown no tendency to drop in recent years. Children make up 36–38% of new cases (all forms), which is substantially higher than the national average, but the incidence of pulmonary tuberculosis shows a progressive shift towards the older age-groups, especially in the male Sardinian.

The hospital stay is now less than a year with 87% of patients and many are now discharged completely cured. An increasing proportion of subjects suffer from chronic forms of the disease. *J. Cauchi*

Romano, S. Aspetti epidemiologici della tubercolosi a Napoli visti dal dispensario "U. Lioy". Nota I. **[Epidemiological Aspects of Tuberculosis in Naples as observed from the "U. Lioy" Dispensary]** *Lotta c. la Tubercolosi.* 1960, Sept., v. 30, No. 9, 801–6.

This tuberculosis dispensary has served the western sections of the City and Province of Naples since 1936; the population of the area was 392,519 in 1958, and their standard of living is on the whole somewhat higher than is to be seen in some other parts of Naples.

At this dispensary, up to mid-1959, 43,783 persons attended for examination and 5,671 of these, from 5,124 households, were found suffering from tuberculosis. 2,053 recovered and 1,334 died.

The record cards of 1,000 patients diagnosed in the 10-year period 1947–1956 showed that 108 came from the middle classes and were not insured; 382 were labourers and 287 of these were insured; 500 others were more or less unemployed and were all insured. There is no certain information as to whether the remainder—10 peasants—were insured. [The insurance status is presumably relevant in that there are probably a number of non-insured persons in the area who may have tuberculosis without coming to the knowledge of the dispensary.] Romano gives percentage figures for tuberculous patients and tuberculous families in relation to rooms per dwelling and persons per room.

J. Cauchi

Andrews, R. H., Devadatta, S., Fox, W., Radhakrishna, S., Ramakrishnan, C. V. & Velu, S. **Prevalence of Tuberculosis among Close Family Contacts of Tuberculous Patients in South India, and Influence of Segregation of the Patient on the Early Attack Rate.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 463–510, 10 figs. [33 refs.]

Owing to the likelihood that treatment with isoniazid of patients in their homes in India will be undertaken on a large scale, it is important to know whether the

isolation of the patients in hospital during treatment will produce a marked fall in the number of cases occurring in the families as contacts. 191 South Indian patients with pulmonary tuberculosis had 693 close contacts. Of these 48·5% were children under the age of 15 years. In a prevalence survey 97% of the contacts had an X-ray examination. Active tuberculosis was found in 6·2% of the males and 7·5% of the females. Of these, 3·8% of the males and 4·5% of the females were excreting tubercle bacilli. The result of initial tuberculin tests with 5 TU of PPD performed on 647 of the contacts showed that 90% of the contacts in the 15–24 age-group already had a tuberculous infection. During the year active tuberculosis developed in 26 contacts, of whom 9 were home contacts (7 were initially tuberculin negative) and 17 sanatorium contacts (5 originally tuberculin negative). The annual attack rate was 14·9% in children of those under the age of 5 years and 6·4% at the age of 5–9 years. 17 (4 home and 13 sanatorium) of the 26 cases arose in the first months. These were attributed to infection by the index case before the start of treatment. 4 tuberculin negative home contacts, and no tuberculin negative sanatorium contacts developed lesions in the second 6 months.

Serial tuberculosis tests made during the year did not yield evidence of more tuberculous infection in the home than the sanatorium contacts. It is concluded that the major risk to contacts during the year resulted from exposure to the index case before diagnosis. The contacts of patients treated at home were not exposed to special risks of infection when compared with contacts of sanatorium patients. *F. H. Young*

COMSTOCK, G. W. & PHILIP, R. N. **Decline of the Tuberculosis Epidemic in Alaska.** *Pub. Health Rep.* Wash. 1961, Jan., v. 76, No. 1, 19–24, 3 figs. [13 refs.]

The first systematic examination for tuberculosis in Alaska was a tuberculin survey made in 1948–51 as part of a BCG vaccination campaign. This showed that the tuberculin reactor rate in children in south-eastern Alaska and the Aleutian islands was 32%, in the interior and on the north-western coast 56% and in the Yukon-Kuskokwim delta 75%.

The delta in which this very high reactor rate was found has an area of about 30,000 square miles and a population of about 7,000 Eskimos and under 1,000 whites. It is the most densely populated area of Alaska. There are 41 villages with populations ranging from 30 to 1,000.

The results of 3 successive tuberculin surveys in the delta are given:

Age	1949–51		1957		1960	
	Total tested	Reactors %	Total tested	Reactors %	Total tested	Reactors %
under 1	88	13·6	46	4·3	84	0
1–2	168	44·0	100	19·0	203	2·5
3–4	168	80·0	96	49·0	177	8·5
5–6	164	90·2	93	74·2	200	33·0
7–8	159	91·8	90	83·3	179	68·8
0–2	256	34·4	146	14·4	287	1·7

These figures show that in 1949–51 the proportion of infected children rose very rapidly with age, in 1957 the increase with age was still evident but much less so, and by 1960 the rates in infants were low but there was still a rapid increase with age.

It appeared that the infection rate was extremely high during the entire lifetime of persons tested in 1949–51 and had fallen but was still high among those tested in 1957. For those tested in 1960 it appeared that the infection rate in recent years was low but had been much higher during the earlier years of the older children.

Because of the rapid change in the infection rate and the influence in some degree of earlier BCG vaccination it was decided to estimate the annual infection rate only on the experience of children under 3 years. The rates prior to the 1949–51 survey, the 1957 survey and the 1960 survey were estimated to be 24·6%, 8·5% and 1·1% respectively.

Other evidence of the marked improvement in the tuberculosis situation in Alaska is provided by the falling tuberculosis death rate from 501 per 100,000 in 1952 to 54 in 1959 and the falling number of admissions to hospital on account of tuberculosis, 1,311 in 1955 and 444 in 1958.

A mass BCG vaccination campaign was carried out in 1949–51 and sporadic vaccination was continued during the following 5 or 6 years but only a small proportion of the population was vaccinated and BCG is not credited with having played an important part in the reduction in tuberculosis.

Because of the likelihood that previously infected persons will provide the cases of tuberculosis in the future controlled trials of isoniazid prophylaxis have been started in which more than 6,000 persons in the delta area are taking part.

The decline in the incidence of tuberculosis appears to be due to social and economic improvement and a vigorous antituberculosis campaign with emphasis on case finding, isolation and treatment.

H. G. Calwell

See also p. 522, PELLETIER, **[Occupation and Pulmonary Disease, especially Tuberculosis. A Survey in the Department of the Seine].**

PARSONS, V. **Awareness of Family and Contact History of Tuberculosis in Generalized Sarcoidosis.** *Brit. Med. J.* 1960, Dec. 17, 1756–9, 2 figs. [13 refs.]

3 unselected series of patients with tuberculosis, sarcoidosis, and asthma and bronchitis were investigated for contact with tuberculosis. Up to 2 years was accepted as the period of contact for the development of tuberculosis, and as far as possible with the incidence of the sarcoidosis. It was found that 12% of the sarcoidosis patients, out of 210, 16% of the 315 tuberculosis patients and only 2% of the 214 asthma and bronchitis patients gave a history of contact.

The author considers that his findings suggest that contact history of tuberculosis is a substantial cause of sarcoidosis which supports the theory that tuberculosis plays a part in the development of sarcoidosis in an appreciable number of patients. *F. H. Young*

McDERMOTT, W. **Antimicrobial Therapy of Pulmonary Tuberculosis.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 427–61. [Numerous refs.]

This paper consists of a review of the present knowledge of the antimicrobial treatment of pulmonary tuberculosis. It is conveniently divided into a number of sections.

(1) Hospital versus home treatment. The author points out that in nearly all patients who are submitted to hospital treatment the second part of the treatment is domiciliary. Hospitalization serves 2 purposes: it provides the only satisfactory opportunity of supervised bed rest, and it removes the infectious patient from his environment. The author considers that the main effect of bed rest without antimicrobial treatment was to reduce the risk of spread from the diseased tissues to new areas of the lung rather than a great advantage in the healing of the original lesion; and that this effect is produced by isoniazid therapy.

Three satisfactory investigations have been undertaken on the problem of the advantage of hospitalization combined with physical rest, and in that undertaken by HIRSCH *et al.* [this *Bulletin*, 1957, v. 32, 740] at the Rockefeller Institute in New York in 1957, patients were submitted to alternating regimes of rest and exercize. Apart from an increased gain in weight during periods of bed rest no advantage appears to have been achieved in the periods of rest compared with the periods of activity.

In the Madras study [*ibid.*, 1960, v. 35, 134], at the end of one year of observation, no appreciable advantage was shown to have been achieved by the patients who were treated in hospital in the groups which were strictly comparable.

In the investigation undertaken by the Tuberculosis Society of Scotland [*ibid.*, 1958, v. 33, 942] comparison was made between patients who were admitted to hospital and those who were allowed to continue at work. Again no advantage was noted in hospitalized cases but the study was confined to patients with non-cavitated disease in a non-infectious state. From the point of view of the spread of infection, it is thought that the advantage of removal of the infective patient from his environment is not overwhelming if adequate precautions are taken with the home contacts.

(2) The choice of chemotherapy of previously untreated patients. The author concludes that pyrazinamide plus isoniazid probably represents the most effective therapy but unfortunately the pyrazinamide is far too toxic for widespread general use. Isoniazid and daily streptomycin is probably the best treatment for patients who are hospitalized. For those for whom this is impossible, isoniazid and PAS is an effective substitute for those patients who can take their PAS satisfactorily without toxic phenomena. Where toxicity occurs the use of isoniazid alone combined with pyridoxine is justifiable; the addition of streptomycin given twice weekly seems hardly worth while.

(3) It is pointed out that the pathological condition in some cavities will probably produce a poor result whatever form of antibiotics are used.

(4) The advantages and disadvantages of the secondary drugs, cycloserine, pyrazinamide, a-ethyl-thioamide, and viomycin are discussed, and their failings pointed out. As their use is usually confined to 3–4 months owing to toxic phenomena it is essential that they should be used with the idea that mechanical methods of treatment should follow if practicable.

(5) The use of steroids in association with antimicrobial therapy is then discussed.

(6) The essential difference between streptomycin-resistant bacilli and those which are resistant to isoniazid is emphasized, with the suggestion that isoniazid-resistant bacilli are not all of the same type.

(7) The paper concludes with a plea that the unfortunate experiences which occurred from the use of unselected cases for pneumothorax treatment before the introduction of antibiotics should not lead to the abandonment of this very useful method of treatment, which in the antibiotic era is largely without risk.

This paper is an admirable review of the present situation as regards antimicrobial therapy of pulmonary tuberculosis. *F. H. Young*

VELU, S., ANDREWS, R. H., DEVADATTA, S., FOX, W., RADHAKRISHNA, S., RAMAKRISHNAN, C. V., SELKON, J. B., SOMASUNDARAM, P. R. & SUBBAIAH, T. V. **Progress in the Second Year of Patients with Quiescent Pulmonary Tuberculosis after a Year of Chemotherapy at Home or in Sanatorium, and Influence of Further Chemotherapy on the Relapse Rate.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 511–33. [20 refs.]

This study is a continuation of one previously made in which the difference in the results obtained by the use of PAS and isoniazid in hospitalized patients and those treated at home were compared [this *Bulletin*, 1960, v. 35, 134]. (This study showed little difference in the results between the 2 groups.)

130 patients in the main analysis were classified as having bacteriologically quiescent disease at the end of the first year. Of these, 126 patients, 61 were allocated at random to calcium gluconate, and 65 to isoniazid—42 having residual cavitation, and 84 showing no evidence of residual cavitation. The patients received 200 mgm. daily of isoniazid for those weighing 100 lb. or more, with reduced doses for those weighing less.

The report endeavours to ascertain: (1) Whether bacteriological relapse and spread of disease are more frequent in patients who attain bacteriological quiescence under treatment at home. (2) Whether in patients who attain quiescence after 1 year's combined chemotherapy, and a second year with isoniazid alone results are superior to those obtained if chemotherapy is stopped at the end of the first year. (3) The influence of residual cavitation at 1 year, the so-called open-negative syndrome on the results in the second year. (4) The progress of the patients whose bacteriological status at one year was in doubt because an isolated positive culture had been obtained in the course of the first year of treatment. 2 (4%) of the home, and 5 (7%) of the sanatorium patients had disease classified as bacteriological relapse;

1 of the home, and 4 of the sanatorium having radiographic deterioration also. 4 patients on calcium, and 3 on isoniazid had relapse bacteriologically; 3 of the former and 2 of the latter with radiographic deterioration also. 1 patient on isoniazid died. Thus, 92% of the calcium patients, and 94% of the isoniazid series had bacteriologically quiescent disease at the end of the second year. It was concluded that the bacteriological status in both groups was very similar at the end of the second year.

Of the 84 patients assessed as having no residual cavity at 1 year, 2 had cavitation at 2 years, and 2 had had a bacteriological relapse with radiographic deterioration. Of 42 patients with cavitated lesions, 1 died, and 3 had their treatment changed. Cavitation disappeared in 6 patients, and was less in 16 others. Of those classified as " bacteriologically of doubtful status " at the end of 1 year's treatment, 1 patient had a bacteriological relapse.

On the evidence available there was no indication that a year's treatment in a sanatorium was able to inculcate regularity in acceptance of the drugs greater than in those who were treated at home. Little evidence was found that the use of 1 year's further treatment by isoniazid produced any great benefit in the prevention of relapse. *F. H. Young*

ROSSI, G., CARANDO-DAMIANO, E., DE MICHELIS, G. & MAGGIOROTTI, P. **Deafness and Vestibular Impairment caused by Strepto- and Dihydrostreptomycin. A Clinical Study about 209 Cases.** *Acta Med. Scandinavica.* 1961, Feb., v. 169, No. 2, 169–80, 7 figs.

" Streptomycin and dihydrostreptomycin can cause serious impairment of the vestibular function and of the hearing. In this study 161 cases of deafness are illustrated, caused for the largest part, by DHSM, and 48 cases of vestibular impairment for the largest part caused by SM. 15 cases of irreversible hearing loss are presented, occurring after administration of small doses of DHSM. The hearing loss due to this antibiotic may be of varying importance and can be divided into 5 types. One of each type is illustrated and the clinical characters and the consequences for the patients' social life are discussed."

BERTE, S. J. & DUNNINGTON, W. G. **An Evaluation of Chemotherapy in Pulmonary Tuberculosis. High Doses of Isoniazid plus PAS versus Low Doses of Isoniazid plus PAS.** *Amer. Rev. Respiratory Dis.* 1961, Jan., v. 83, No. 1, 50–56.

This paper compares the results of 2 groups of patients at the end of 3, and 5 to 6 months' treatment respectively. 91 patients were treated with conventional doses of isoniazid 300 mgm. daily, plus PAS 12 gm. daily. These were compared with 113 patients who had been treated with high doses of isoniazid 10 to 20 mgm. per kgm. daily, PAS 12 gm. daily, and pyridoxine 100 mgm. daily. Classification is made into the moderately and far advanced cases and the single and multiple cavity cases. The groups seem fairly comparable with a slight bias in favour of the high-isoniazid-PAS group.

Estimation of the concentrations of free isoniazid in the serum was made by biological methods, and it was found that in the high isoniazid group 22% of patients, and in the low isoniazid group 45·6% of patients had serum concentrations below 0·6 μgm. per ml.

Tables give the bacteriological results for all cases, for cases classified as moderately and far advanced, and according to number and progress of cavities. Generally speaking it was found that although the number of patients with negative cultures was rather larger in the high isoniazid group at the end of 3 months, there was little difference between the 2 groups at the end of 6 months. The same lack of difference was found in the percentage of patients whose cavities closed. No statistically significant difference was found between the results in the 2 groups either with those with serum isoniazid concentrations below 0·6 μgm per ml. or those with concentrations above this figure. Again, tested by the extent of radiological improvement, no significant difference was found between the 2 groups.

Although not statistically significant, it was found that among the more rapid inactivators of isoniazid 13·1% more cavities closed in the low-isoniazid-PAS group, whereas among the slower inactivators of isoniazid 10·3% more cavities closed in the high-isoniazid-PAS group. Hence the rate of closure of cavities on any dosage of isoniazid is not related to the concentration of free isoniazid in the serum as determined microbiologically 6 hours after an oral dose of the drug. The authors suggest that possibly the dosage in the high isoniazid group was not sufficiently high.

The authors conclude that they were unable to demonstrate that there is any advantage in the high isoniazid group when tested under the conditions detailed in this paper. They feel that a small group of patients including those who inactivate isoniazid rapidly, those with cavity disease, and previously untreated patients who have had productive pulmonary lesions for a long time may be benefited by high dosage treatment. [See also this *Bulletin*, 1960, v. 35, 776.] *F. H. Young*

UNITED STATES PUB. HEALTH SERVICE: **Tuberculosis Therapy Trials. Long-Term Consequences of Isoniazid Alone as Initial Therapy.** *Amer. Rev. Respiratory Dis.* 1960, Dec., v. 82, No. 6, 824–30. [10 refs.]

In a study of the 3 standard regimes in 1952 by the Public Health Service of the United States it was decided to try to examine the state of the patients at the end of 5 years. 411 patients were available for evaluation, of whom 150 had been treated by isoniazid alone, 131 by isoniazid + streptomycin, and 130 by streptomycin and PAS. These patients had had 40 weeks of antimicrobial therapy.

On the examination of their condition at 5 years, the patients were classified as bacteriological failures and bacteriological successes after 40 weeks of treatment. Failures included those still infectious or whose regime had been changed, and those who died of tuberculosis during treatment. Failures numbered 49 on isoniazid

alone, 13 on isoniazid and streptomycin, and 27 on streptomycin and PAS. Patients whose sputum did not yield tubercle bacilli on culture after the 32nd week are considered as successes—101 on isoniazid, 118 on isoniazid and streptomycin, and 103 on streptomycin and PAS.

Various methods of treatment were given to the failures after their 40 weeks' treatment. Including the deaths during control therapy, one-fifth of the isoniazid failures had died of tuberculosis, compared with one-tenth of the streptomycin-PAS failures and no deaths among the isoniazid-streptomycin failures.

Of the bacteriological successes, 74·2% of the isoniazid, 73% of the isoniazid-streptomycin, and 74·7% of the streptomycin-PAS groups were known to have had inactive disease at the end of the 5 years. The authors conclude that among patients who are bacteriological successes at the end of 40 weeks there was little difference attributable to the various combinations of drugs which they had received for the first 40 weeks. Patients who had received isoniazid alone did as well as those who had received combined therapy.

Although the bacteriological failures were small in number, there was some indication that patients who were still infectious after 40 weeks of treatment with isoniazid alone had a less favourable prognosis than failures on combined therapy. *F. H. Young*

Bull. World Health Organization. Geneva. 1960, v. 23, Nos. 4/5, 535–85, 3 figs. [53 refs.] **A Concurrent Comparison of Isoniazid plus PAS with Three Regimens of Isoniazid alone in the Domiciliary Treatment of Pulmonary Tuberculosis in South India** [Tuberculosis Chemotherapy Centre, Madras.]

This paper from the Madras Tuberculosis Centre compares the results of the treatment of Indian patients on 4 regimes. It deals with 90 patients who were given a mean daily dose of isoniazid of 4·6 mgm./kgm. body weight plus sodium PAS 10 gm. a day in 2 equal doses (PH). 70 patients received isoniazid alone, an average of 8·7 mgm./kgm. body weight daily in 1 dose (HI–1); 68 patients received the same amount of isoniazid (alone) but in 2 doses (HI–2) and 87 patients received isoniazid alone, 4·5 mgm./kgm. a day in 2 equal doses, graded according to the patient's weight (H). At the end of 12 months all patients could be re-examined. Most patients showed at least moderate radiographic improvement; 85% of the PH series, 78% of the HI–1; 71% of the HI–2, and 62% of the H series. Disappearance of cavitation appeared in a similar ratio. The cultures from 90% of the PH, 76% of the HI–1, 59% of the HI–2, and 51% of the H series were negative at the end of 12 months. From the end of 6 months onwards nearly all positive cultures in all 4 series were isoniazid-resistant.

Peripheral neuritis attributed to isoniazid occurred in 1% of the PH, 19% of the HI–1, 9% of the HI–2, and none of the H patients. In all series patients with primary isoniazid resistance did badly. The self-administration of the cachet and tablets was checked by tests on the urine; there were only minor differences between the 4 series in the proportion of patients with negative results. Urine tests for the regularity of the taking of the drugs were performed in a number of cases but at routine visits only about 5% of the patients were convicted of failing to take their drugs and surprisingly the proportion was about the same with the PAS/isoniazid series as the isoniazid alone series. The high proportion of patients with isoniazid-resistant bacilli at the end of 6 months makes the results of these tests rather suspect.

The study confirms that the combination of isoniazid plus PAS for 12 months is satisfactory domiciliary treatment in Madras city. Of the isoniazid alone regime the single daily dose of 8·7 mgm./kgm. (HI–1) was the most satisfactory but the incidence of peripheral neuritis was considerable.

This appears to have been a well conducted survey and a large number of supporting tables are appended. *F. H. Young*

Devadatta, S., Gangadharam, P. R. J., Andrews, R. H., Fox, W., Ramakrishnan, C. V., Selkon, J. B. & Velu, S. **Peripheral Neuritis due to Isoniazid.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 587–98, 1 fig. [24 refs.]

This paper reports the peripheral neuritis which appeared during the trial of 4 different regimes reported above from the Madras Tuberculosis Centre. The time of onset of symptoms of peripheral neuritis ranged from the 2nd to the 10th month of treatment, and was earlier in the HI–1 patients than in the HI–2 patients. 9 patients were treated with pyridoxine and gradual improvement was noted. 7 patients were treated with vitamin B complex, 6 continued on isoniazid, the dose being lowered in some; all 7 patients improved. This drug was very much cheaper than pyridoxine. Serum isoniazid assays were performed on 143 of the 148 patients allocated to the HI–1 and the HI–2 regimes. 19 patients with peripheral neuritis had a higher mean serum level of isoniazid than the 124 patients who did not develop this complication. The difference between the incidence of peripheral neuritis in the slow and the rapid inactivators of isoniazid attained statistical significance. *F. H. Young*

Butt, H. Klinischer Erfahrungsbericht über die Kombinationsbehandlung der Lungentuberkulose mit Cycloserin-Pyrazinamid. **[Clinical Experiences in the Treatment of Pulmonary Tuberculosis with a Combination of Cycloserine and Pyrazinamide]** *Wien. med. Woch.* 1961, Jan. 21, v. 111, No. 3, 57–61. [35 refs.]

The author has treated 27 patients suffering from pulmonary tuberculosis with cycloserine since the beginning of 1959. The preparation used was cycloserine tartarate (Pfizer).

3 of the patients were treated only after a short period, and the results in the remaining 24 cases were analysed. The duration of the illness ranged from 2½ to 16 years. Specific treatment had been given, and in most cases there was clinical resistance to streptomycin, PAS or isoniazid. Cycloserine by itself was not given to any patient.

The forms of tuberculosis present are described. 16

patients were given cycloserine with pyrazinamide from the start, 3 were excluded as mentioned above, and the remaining 8 were considered separately for reasons stated.

The dosage of cycloserine was 625–1,000 mgm. and of pyrazinamide 1–1·5 gm daily. The results were assessed radiologically, bacteriologically, clinically and biochemically; complications of the treatment were also recorded.

Only 1 of the 16 patients had no cavitation; the cavities disappeared in 2, were markedly reduced in size in 4, moderately reduced in 5, remained unchanged in 4 and increased in none. There was complete resolution of the tuberculous lung foci in 2 patients, distinct regression in 10, moderate regression in 1, no change in 3 and worsening in none.

The erythrocyte sedimentation rate fell to normal in 6, was much reduced in 6, unchanged in 2 and showed a rise followed by a fall in 2.

All the patients were sputum-positive at the start; sputum conversion was found in 5 after 1 month, in 3 after 2 months and did not occur in 5. 3 patients were discharged prematurely so that the state of their sputum could not be ascertained. Relapse was not found to occur in the patients who had undergone sputum conversion.

There was evidence of liver dysfunction in 10 patients at the beginning. Mild jaundice occurred during the course of treatment in 1 patient; the drugs were withheld and glucose and liver hydrolysate given with good effect so that the treatment was restarted and continued without relapse.

In 1 patient, whose blood sugar had been normal at the beginning, symptoms of diabetes mellitus appeared in the 4th month, and his blood sugar was found to be 280 mgm.%. The withholding of cycloserine and pyrazinamide and the administration of a suitable diet failed to produce a normal blood sugar level. Specific treatment (Nadisan (carbutamide) 3 tablets daily) was then given for the diabetes with success, and the antituberculous drugs were resumed. Hypoglycaemia ensued and the dose of Nadisan had to be reduced to 1 tablet daily. The effect of cycloserine in reducing the level of the blood sugar has previously been described but the author is not aware of any report of the appearance of diabetes during treatment with cylcoserine.

There was no evidence of a toxic effect on the blood or kidneys.

In the group of 8 patients mentioned separately 1 who received cylcoserine and pyrazinamide had been treated at the beginning by the author with pyrazinamide and viocin, 2 with a combination of streptomycin, PAS and isoniazid and 1 with streptomycin and isoniazid. 3 were treated from the start with cylcoserine and isoniazid and 1 with cycloserine and Marsilid. Treatment with cycloserine in this group continued for 1½–3 months. Details of the cases are given. There was a good result in 6 patients (75%) and sputum conversion occurred in 5 (62·5%).

Side effects were seen in 12 of the 27 patients (44·4%). They were severe enough to necessitate withdrawal of the cycloserine in 4 (14·8%), but in the others temporary withdrawal and treatment with a sedative drug enabled the treatment to be continued. No clear connexion between dosage or duration of administration and the frequency of side effects was found. There is a probability that their incidence is connected with the duration and extent of the lung lesions.

Butt concludes that cycloserine is a valuable drug in cases of resistance to the "classical" tuberculostatic drugs.

H. G. Calwell

HAAPANEN, J., GILL, R., RUSSELL, W. F., Jr. & KASS, I. **Re-Treatment of Pulmonary Tuberculosis. Experiences with Various Combinations of Pyrazinamide, Cycloserine, and Kanamycin in Patients excreting Tubercle Bacilli resistant to both Streptomycin and Isoniazid.** *Amer. Rev. Respiratory Dis.* 1960, Dec., v. 82, No. 6, 843–52. [16 refs.]

Between October 1st, 1954, and October 1st, 1958, 171 adult patients excreting typical mammalian tubercle bacilli resistant to both streptomycin and isoniazid were treated for 6 months or longer at the National Jewish Hospital at Denver, Colorado. Re-treatment of these patients with isoniazid, and a combination of streptomycin or PAS or both produced 9% reversal of infectiousness without other drugs or surgery. In another 14% surgical treatment in addition to the antimicrobial treatment resulted in reversal of infectiousness. In 77% the sputum remained positive. Between April 1958 and May 1960, 2 studies were undertaken, which included 47 and 18 patients respectively who were excreting resistant organisms. They were all classified as moderately or far advanced.

In the first study the 47 patients were divided into: Group A, patients who received kanamycin, pyrazinamide and cycloserine. Group B, patients who received pyrazinamide and cycloserine. The dosage of pyrazinamide was 0·5 gm. 3 times daily by the mouth, and that of cycloserine 250 mgm. twice daily by mouth. In most cases the therapy was continued for at least 6 months. Kanamycin sulphate 1·0 gm. daily was administered by the intramuscular route 4 or 5 days a week for a period averaging 5 months.

In the second study of 18 patients they were divided into Group C, patients who received cycloserine and pyrazinamide, and Group D, patients who received kanamycin and pyrazinamide. The dosage of cycloserine was increased to 0·5 gm. daily, and the pyrazinamide dosage increased to 40 mgm. per kgm. not exceeding 3·1 gm. divided into 3 doses daily. The kanamycin therapy was continued as already outlined. In addition, PAS and isoniazid were continued. Pyridoxine 50–300 mgm. daily was given and sometimes meprobamate, perphenazine and chlorpromazine were used in addition in an effort to prevent the toxic side effects of cycloserine. Serum assay studies were undertaken in many cases.

Of the 26 patients in Group A, reversal of infectiousness was obtained by drugs only in 7; in 7 reversal was obtained but they had in addition prophylactic surgery; in 4, reversal of infectiousness occurred only after surgery. In 8 patients sputum was persistently positive either with drugs, or drugs and surgery. In Group B, the results were 10, 1, 1, and 9 respectively. In group C, non-infectious sputum was obtained in 7 patients out

of 8, 1 remaining positive. In Group D, reversal was obtained by drugs in 2 patients, with surgery in addition in 1 patient, and 7 remained persistently positive. Significant drug reactions occurred among the 65 patients as follows: cycloserine—14 patients; pyrazinamide—12 patients; kanamycin—auditory toxic effects in 6.

In the study on the 47 patients the absence of success with drugs which are known to be sterilizing agents for tubercle bacilli suggested that the drugs were not delivered adequately. The correlation of bacteriological and serum studies showed that in almost all cases the patients were not receiving enough cycloserine or kanamycin. In the second group of 18 patients, the improvement in results confirms this idea. In addition the use of kanamycin does not seem to add any considerable benefit. It seemed, therefore, that the use of adequate doses of pyrazinamide and cycloserine will produce favourable results in a high proportion of the drug-resistant patients, provided that adequate doses of the drugs are delivered. Toxic reactions, however, may prevent this end being achieved, though the use of meprobamate 800–1,200 mgm. per day and pyridoxine 300 mgm. per day appears to deal with this difficulty in most cases. Marked hepatocellular damage was observed in only one of the patients and this was proved to be reversible.

This is a very valuable and interesting paper.

F. H. Young

Ollagnier, C. & Colas, A. Etude à court terme du traitement de la tuberculose par l'éthioniamide (1314 Th). [**Short-Term Study of the Treatment of Tuberculosis with Ethioniamide (1314 Th).**] *Maroc Méd.* 1960, June, v. 39, No. 421, 647–65. [Numerous refs.]

Ethioniamide (1314 Th) [this *Bulletin*, 1959, v. 34, 621] is one of the recently introduced anti-tuberculous drugs, and this paper studies its use. The average dose used was 1 gm. in 4 doses daily. In some patients 2 suppositories of 0·5 gm. were used daily. The number of patients treated was 83 of whom 46 (56%) lost little weight; 23 (27%) had a considerable loss of weight; 24% had troublesome digestive symptoms, but none developed ulcers. Other toxic symptoms were infrequent.

A very elaborate analysis of results is given, dividing the patients into longstanding and recent cases and into classifications according to resistance. This reduces the numbers too greatly to allow great weight to be given to the conclusions. The authors consider that the drug is a useful addition to the armamentarium against tuberculosis, especially where resistance to other drugs exists. A complete bibliography is appended. *F. H. Young*

Horne, N. W. **Prednisolone in Treatment of Pulmonary Tuberculosis: a Controlled Trial. Final Report to the Research Committee of the Tuberculosis Society of Scotland.** *Brit. Med. J.* 1960, Dec. 17, 1751–6, 2 figs.

This paper gives the final report on the use of prednisolone in the treatment of pulmonary tuberculosis by the Research Committee of the Tuberculosis Society of Scotland [this *Bulletin*, 1958, v. 33, 111].

178 patients were treated with chemotherapy on the usual standard lines. Of these, 87 were given in addition prednisolone in a dosage of 20 mgm. daily for 3 months. The patients in the control group and the prednisolone group seem to have been evenly matched. The observation in all cases was 12 months. Under the classification of the U.S. National Tuberculosis Association 48% of the patients had far advanced disease, 47% moderately advanced disease, and 5% minimal disease.

154 of the patients were sputum-positive with organisms sensitive to streptomycin, PAS, and isoniazid. In the prednisolone group there was a more rapid gain of weight, and a more rapid reduction of sedimentation rate. This difference of weight levelled out at the end of about the third month, but persisted to the end of 6 months. The fall in the sedimentation rate levelled at the end of 4 months, and at the end of 6 months was approximately the same. The improvement in the X-ray shadows in the prednisolone group were statistically highly significant at the first, second and third months, and significant at the fourth month. An endeavour was made at the end of 12 months to estimate the average residual opacity in the radiographs. With prednisolone it was 18% in the original, and in the control group 24%. The figures for cavity closure were approximately the same in both groups. At the end of the 6th month 100% of the control group and 99% of the prednisolone group had achieved sputum conversion, but in the first 3 months the rate of conversion was considerably greater in the prednisolone group.

Toxic effects were similar in both groups. Cessation of prednisolone therapy on account of serious toxic effects was necessary in only 2 cases; in 1 glycosuria and a diabetic curve were revealed, and the second showed a marked rise of diastolic blood pressure to 140 mm. in the 6th week of treatment.

The author concludes that no serious toxic effects arise from the use of the prednisolone. The rate of reduction of toxaemia is appreciably greater in the prednisolone group, and both conversion of sputum and reduction of radiological shadows occur earlier in this group. There was some evidence that at the end of 12 months fewer residual shadows were present in the prednisolone group than in the control. *F. H. Young*

Marcus, Henriette & Christopoulos, P. **Antimicrobial-Steroid Treatment of Active Pulmonary Tuberculosis as a Routine Measure.** *Arch. Intern. Med.* 1960, Apr., v. 105, No. 4, 542–59, 10 figs. [26 refs.]

This paper deals with 30 patients, most of whom were negresses who had far advanced tuberculosis, some with additional complications; in nearly all the duration of the disease was less than 6 months. They were given antimicrobial treatment, and in addition were given prednisone or prednisolone in doses varying from 600 to 1,000 mgm. a month; it was thought that 600 mgm. was the minimum dose for full therapeutic effect. Notes of 30 patients previously treated with the same type of antimicrobial treatment were extracted at random from the files as a method of comparison. As they were not matched, they cannot be considered a full control series.

A diagram is given showing the X-ray clearing at 4, 8, 12 weeks, and the final result, but the exact duration of treatment is not given. Compared with the so-called control group the rapidity of clearing was very marked. The final result showed 17 patients with very marked clearing, 10 with marked clearing, 3 with moderate clearing, and 1 who died. The final result in the control group was: 3 with very marked clearing, 8 with marked clearing, 14 with moderate clearing, 2 with no change, 3 died.

The duration of the steroid therapy depended on the rapidity of the clearing, and varied from 31 to 188 days. Some details of the 30 cases are given, and 5 illustrative cases are reported more fully. The one fatality was in a patient with advanced disease, admitted moribund, who did very well until she developed massive gastro-intestinal bleeding. This was treated, but it was also found that she had developed diabetic coma, though on admission two urinalyses and one blood sugar determination had been normal. As a result of these complications the steroid therapy was tapered off and discontinued within 10 days, and within a few days of the termination of therapy the patient became acutely febrile and developed rapidly progressive pulmonary tuberculosis and died. Care was taken to discontinue the steroids slowly.

The authors consider that there are a few contra-indications to the administration of steroid hormones. Peptic ulcers must be treated carefully, and other infections must be treated by the appropriate antibiotic. They consider that the steroid therapy ought to be started immediately on admission, as if it is postponed less dramatic results are obtained. The authors consider that combined steroid and antimicrobial therapy is at present the best form of treatment for all patients with active tuberculosis, provided that the patient is not resistant to the antimicrobials prescribed. The results described in this paper differ from those described by many other authors who consider that the final result is not much influenced by the steroid therapy though the effects early in treatment are very dramatic. *F. H. Young*

HAMLIN, L. E. **Rehabilitation of Foundry Workers with Active Pulmonary Tuberculosis. A Study of 21 Employees over a Period of 10 Years.** *Indust. Med. & Surgery.* Miami. 1960, Oct., v. 29, No. 10, 453–60, 7 figs.

After some preliminary remarks on the incidence of tuberculosis in foundry workers the fate of 21 workers who developed pulmonary tuberculosis is reported. All except 1 were diagnosed as a result of regular mass X-rays provided by the management. 6 patients had dust disease complications, but no patients with advanced disease were discovered.

Of the 21 patients, 12 were able to be employed at regular jobs, and 2 at light jobs after treatment; 1 died of an accident, 3 were not doing full work because of other diseases, and 3 had left the industry but were reported as being well. Over 90% of the patients were over 40 years of age at the time of diagnosis. Illustrative case histories are given. *F. H. Young*

LINCOLN, Edith M., SORDILLO, S. V. R. & DAVIES, Pamela A. **Tuberculous Meningitis in Children. A Review of 167 Untreated and 74 Treated Patients with special reference to Early Diagnosis.** *J. Pediatrics.* St. Louis. 1960, Dec., v. 57, No. 6, 807–23, 3 figs. [19 refs.]

Based on the observation of 241 children who were diagnosed in the Chest Clinic of the Bellevue Hospital, New York, as having tuberculous meningitis, this paper gives an excellent account of the disease.

167 children were seen before specific therapy was available [this *Bulletin*, 1948, v. 23, 19], and 74 were treated by antimicrobial therapy between 1947 and 1956. As in the early part of the investigation the most up-to-date methods of antimicrobial therapy were not available, the actual results are not so important as the conclusions drawn. The prognosis was found to depend: (1) On the stage of the disease at the onset of therapy, and (2) the age of the child. Early diagnosis is therefore essential, and this paper brings out many of the points which are valuable in early diagnosis. The following are the most important.

Tuberculosis should always be suspected as a cause of fever, etc. during convalescence from measles. Symptoms of upper respiratory infection frequently obscure early tuberculous meningitis. The most frequent initial symptoms are fever, vomiting, apathy and anorexia.

Of 48 patients treated for tuberculous meningitis, 47 had a positive tuberculin test at the time of the menin gitis. 75% of chest X-rays showed evidence of primary tuberculosis and an additional 14% calcified or calcifying disease.

The closing date (1956) makes the results a little out of date but the paper gives an admirable account of tuberculous meningitis in children with most valuable hints on early diagnosis. *F. H. Young*

NICKERSON, G. & MACDERMOT, P. N. **Psychometric Evaluation and Factors affecting the Performance of Children who have recovered from Tuberculous Meningitis.** *Pediatrics.* Springfield, Ill. 1961, Jan., v. 27, No. 1, 68–82. [19 refs.]

The authors point out that medical literature abounds with reports of patients who have survived tuberculous meningitis, but little substantial information has been given regarding their intellectual capacity. Psychometric testing was done on 50 children who had recovered from tuberculous meningitis. The children to be tested were brought to live in a specially prepared and attractively equipped ward, in groups of similar ages and with friends whom they had made while in hospital. The children were permitted 3 days to familiarize themselves with the ward, with one another, and with the psychologist by talking and playing. One or both parents were interviewed in an attempt to add information as to the child's abilities before his illness. A list of the recognized tests employed is given.

Tests under control conditions revealed that the group as a whole was below average in intelligence. 5 were of high average intelligence, 10 were average, 12 were dull normal, and 7 were borderline normal. 16 were

mentally deficient in varying degrees. Electro-encephalographic findings in all patients, undertaken at one time or another, revealed some degree of cerebral dysfunction. The mean IQ for the 50 children was 73·02 ± 3·88, which is significantly lower than the standard value of 100.

The following factors are discussed. It was found that in a group of children with mental deficiency there was an average age of 2·8 years at onset of the disease, whereas the average age of onset of children who retained borderline intellect or better was 6·2 years.

Rather surprisingly it was found that early diagnosis did not produce any significant difference; nor did unconsciousness. On the other hand the appearance of convulsions was important. The mean IQ of 19 patients with convulsions was 57·63 ± 7·29; that of the 31 without convulsions was 82·45 ± 3·50. Observation suggested that unconsciousness and convulsions were to a large measure directly associated with the degree of intracranial pressure. Accordingly efforts were made to alleviate this. Cranial burr holes were found to have certain elements of danger and were abandoned. Acetazoleamide (Diamox) and adrenal corticoids were not found to be of any material benefit. Repeated lumbar puncture in most cases seemed to be the safest and most reliable method of controlling intracranial pressure.

The following factors were thought to be detrimental to recovery:—Prolonged isolation due to hospitalization, sensory-motor sequelae, and unfavourable social circumstances. 5 of the 7 patients with borderline intelligence were Eskimoes who lived a nomadic existence, whereas the other 2 came from unusually poor homes. Without exception the children who exhibited evidence of emotional insecurity on testing came from insecure home environments.

Repeated psychometric testing did not show much difference when the tests were carried out 1½ to 3½ years after the first testing, but in 9 patients changes in performance were noted; 7 of these patients showed improvement, whereas 2 performed less well.

F. H. Young

GRIFFITHS, Margaret I., BRINDLE, T. W., GORDON, E. H., HOLME, T. & JONES, Barbara. **Multiple-Puncture Vaccination with Freeze-Dried B.C.G. Vaccine in Schoolchildren.** *Brit. Med. J.* 1961, Feb. 25, 536–40, 4 figs. [18 refs.]

The aim of these trials was to compare the results of multiple-puncture with those of intracutaneous BCG vaccination and to attempt to assess some of the factors which influence the effects of multiple-puncture vaccination. British freeze-dried vaccine was used. [See also this *Bulletin*, 1959, v. 34, 879; 1960, v. 35, 882.]

In the first trial the effects of vaccine strength of 83 mgm./ml. given by multiple puncture, with 20 needles at depths of 2 or 3 mm., were compared with those produced by intracutaneous vaccination with vaccine of a strength of 500,000 viable organisms per dose.

The pre-vaccinal test was the Mantoux test with 10 TU of OT, and the criterion of a positive reaction was induration of 5 mm. or more. Of 1,099 schoolchildren tested 791 were non-reactors and were vaccinated either intracutaneously or by multiple-puncture at 2 mm. or 3 mm. in strict rotation. The technique is described. The vaccination sites were inspected 6 weeks later and the Mantoux test repeated at that time and 1 year later. The results were:

Method	Results to 10 T.U.							
	Dr. A		Dr. B		Dr. C		Dr. D	
	Mean Diam. (mm.)	% Pos.	Mean Diam. (mm.)	% Pos.	Mean Diam. (mm.)	% Pos.	Mean Diam. (mm.)	% Pos.
6 Weeks								
Intradermal	20·7	100	13·0	99	10·1	94	8·9	100
Multiple puncture, 20/2 mm.	18·8	100	9·6	90	7·7	83	7·0	88
Multiple puncture, 20/3 mm.	18·5	100	9·6	91	8·2	92	8·2	93
1 Year								
Intradermal	21·7	100	10·7	84				
Multiple puncture, 20/2 mm.	20·1	94	5·2	51	Not tested			
Multiple puncture, 20/3 mm.	20·2	100	5·0	44				

It was found that there were marked variations between the results produced by the 4 investigators but in all 4 instances the intracutaneous technique gave higher conversion rates than multiple puncture. In none was there any significant difference between the effects of multiple puncture at 2 mm. and 3 mm.

In the 2nd trial a specific problem was assigned to each investigator thus eliminating the variable factor of operator technique in each group. During this trial 2,422 children were tested and 1,744 non-reactors to 10 TU vaccinated. The following factors were assessed: the effect of heat on the vaccine, differences in strength of vaccine, the effect of roughened needles, types of guns and variations in pressure and correlation of local reaction and degree of post-vaccinal tuberculin sensitivity.

It was found that heating the gun had a deleterious effect on the vaccine and adequate time for cooling must be allowed if this method of sterilization is used. No difference in the rate of tuberculin conversion was found with vaccines of 83 mgm./ml. and 125 mgm./ml. Roughening of the needles had no effect on the conversion rate. The results obtained with various guns suggested that a pressure between 5 and 9 pounds (2·3 and 4 kgm.) was adequate to fire 20 needles 2 mm. into the skin. In all cases a degree of local reaction producing pustules, scaling, or confluence was associated with tuberculin conversion equivalent to that produced by intracutaneous vaccination.

H. G. Calwell

PARROT, L., CATANEI, A., LAVERDANT, C. & GARRIGUES, P. Sur un essai de vaccination antituberculeuse itérative (2e note). [**A Comparison of Post-Vaccinal Allergy in Infants Vaccinated with BCG by Scarification and Repeated Oral Administration**] *Arch. Inst. Pasteur d'Algérie.* 1960, Dec., v. 38, No. 4, 484–6.

In an earlier communication [this *Bulletin*, 1959, v. 34, 624] Parrot and the next two above-named authors

reported that in a group of 33 infants, of whom 17 were vaccinated with BCG by scarification and 16 by repeated oral administration, the reactor rates to the BCG test 26 months after vaccination were 89·4% and 82·6% respectively. No case of anergy due to desensitization by repeated vaccination was seen.

The period of observation has now been extended to 50 months, and 23 of the original group of 33 infants have been retested; 13 of 14 vaccinated orally and 8 of 9 vaccinated by scarification were found still positive to the BCG test.

The authors therefore adhere to their original conclusion that vaccination by repeated oral administration is not superior to vaccination by scarification which is the method of choice for mass vaccination, at least in the rural areas of Algeria. *H. G. Calwell*

VENEREAL DISEASES

NICOL, C. S. **The Recrudescence of Venereal Diseases.** *Brit. Med. J.* 1961, Feb. 18, 445–7, 1 chart. [31 refs.]

Few people can be more fitted to report on the increase of venereal diseases than Dr. Nicol. Though new cases of reported syphilis and chancroid in clinics in England and Wales have fallen from 8,432 and 453 to 3,927 and 267 respectively between 1951 and 1959, gonorrhoea has risen from 18,064 to 31,344 and non-gonococcal urethritis from 10,794 to 20,227; these are of course not the true figures since patients seen by private practitioners are not included and there is reason to believe that these too have risen.

The explanation is partly due to immigration (mainly from the West Indies) and also no doubt to increasing promiscuity resulting from the encouragement of books, papers, magazines, films and television programmes.

Though cases of reported syphilis have decreased the decrease may be more apparent than real because the indiscriminate use of antibiotics, especially penicillin, for all sorts of conditions may well have masked cases of incubating syphilis. It is of interest to note that not a few cases of early syphilis have occurred in homosexuals. Latent syphilis seems likely to increase; since this condition can only be diagnosed by blood tests, the introduction of the treponemal immobilization test is of great importance but where this is not practicable the Reiter protein complement-fixation test is indicated. The increase of gonorrhoea may be explained in several ways; easy and rapid cure means repeated reinfection, the influx of immigrants and the tendency of gonococci to show some resistance to penicillin; moreover reservoirs of infection (in women) are hard to find and teenagers seem to be increasingly involved [this *Bulletin*, 1960 v. 35, 1109].

In addition to the above, non-gonococcal urethritis is difficult to treat successfully and trichomoniasis (which frequently follows sexual intercourse) has hitherto presented a serious problem: however the introduction of Flagyl (metronidazole) holds out great hopes [*ibid.*, 1961, v. 36, 145].

Of other venereal diseases lymphogranuloma venereum, granuloma inguinale and chancroid are comparatively rare though the first named may be introduced by coloured immigrants.

The solution to the whole problem lies in tracing and treating infected contacts; for this the services of a social worker are essential; if practitioners would send their patients to the nearest clinic for diagnosis, before giving (antibiotic) treatment, a good deal of time and trouble would be saved.

[See also this *Bulletin*, 1958, v. 33, 654.]

T. E. Osmond

KOTARIYA, V. T. **[Repeated Affection with Syphilis]** *Vestnik Dermat. i Venerol.* Moscow. 1961, v. 35, No. 1, 52–4. [In Russian.]

The English summary appended to the paper is as follows:—

"During a 9-year period the author observed 24 patients who repeatedly fell ill with syphilis. According to the treatment schemes accepted in the USSR 18 patients out of 24 underwent a complete course of treatment. Not a single patient with reinfection was admitted to the hospital, even after an obviously unsatisfactory treatment, particularly following arsenoxide therapy, although this mode of therapy was widely employed during 1946—1948. The observed cases of syphilis reinfection show that the Soviet schemes for the treatment of syphilis have fully justified themselves."

LO MONACO, G. B. Indagini sierologiche per l'accertamento della lue. Bilancio di un anno (1959) di applicazione a Firenze della legge 25 luglio 1956 n. 837. **[Records of One Year's (1959) Observations in Florence in Application of the Law of 25th July 1956; n. 837]** *Riv. Istituto Sieroterap. Ital.* 1960, July–Aug., v. 35, No. 4, 440–58. [46 refs.] English summary.

The Italian Law 837 of 25/7/56 on "Reform of legislation in force for the prophylaxis of 'venereal diseases" lays down the various circumstances in which a certificate of serological examination of the blood for evidence of syphilis must be obtained (intention to marry, military service or imprisonment). And in July 1960 it was further laid down that this examination should take the form of a flocculation reaction with cardiolipin antigen followed, where the serum was positive or weakly positive, by a complement-fixation reaction [CF] with both cardiolipin and purified trepomonal antigens. The latter are obtained from cultures of

Reiter treponemata by the method of D'Alessandro and Dardanoni [*Riv. Istituto Sieroterap. Ital.* 1952, v. 28, 153; this *Bulletin*, 1953 v. 28, 702].

The author's observations are recorded with a view to assessing the value of the various procedures in use during the year 1959 in Florence in carrying out examinations in accordance with the new law.

The reactions carried out were: the micro flocculation test, VDRL; complement fixation (a) with cardiolipin antigen, (b) with purified Reiter trepomone antigen; and the Meinicke II reaction.

1,077 cases from prisons, hospitals, etc. gave 16% positive. 10,247 sera from "normal" persons gave 1·8% positive. Among the positive reactors in both groups a considerable proportion were submitted to careful clinical examination and their antecedents were taken into account.

From these investigations it appeared that 43% of the normal with positive reaction gave evidence of syphilis, 36% were dubious cases of syphilis and 21% were false positives. In the group from prisons and hospitals 81% appeared to be cases of syphilis, 8% doubtful cases of syphilis and 11% false positives. As assessed by comparing clinical findings in cases in which one only of the reactions gave a positive result, it appeared that the micro flocculation test was the most valuable and the Mk. II the least.

A combined positive with CF depending on Reiter antigen and one or more positive lipoid antigen reactions gave very close correspondence with the clinical findings.

J. W. McLeod

Mirdamadi, H. **A Rapid Method of Complement Fixation Test for Syphilis.** *Acta Med. Iranica.* 1959, Sept., v. 3, No. 1, 35–48, 3 figs. [18 refs.]

The reaction described in this article is on the usual lines but with several differences; the most important of these are (1) use of flat bottomed tubes (9 × 1·5 cm.) with a glass bead at the bottom, (2) shaking at 150–180 r.p.m. for 10 minutes (the author points out that excessive shaking may damage the complement), (3) incubation for 10 minutes at 35°C. after serum and antigen have been mixed, again in a similar way after addition of complement and a third time after addition of the sensitized cells. Cardiolipin-lecithin-cholesterol antigen is used (0·03%, 0·2% and 0·9% respectively) or alternatively Reiter's treponeme antigen. Complement and haemolysin (rabbit anti-sheep) are titrated in the usual way, saline is 0·85% and sheep cells 2%. Quantitative tests can be carried out by making serial dilutions of the test serum 1/4, 1/8, 1/6 [? 1/16], 1/32, 1/64 and 1/128. Serum is used in amounts of 0·05 cc. and cerebrospinal fluid 0·5 cc.

The above test (MCFT) was compared with Kahn, Müller, Meinicke and Müller-Wassermann on 901 sera; all were negative in 351 and positive in 483; there were 67 discrepancies, 30 of which were positive with MCFT and negative with the other tests and 37 negative with MCFT and positive with the others. Of the 30, 23 were positive with TPI, 5 were probably syphilitic and the other 2 were "cerebral insultus" and intercostal neuralgia.

Of 171 sera positive with TPI, 102 were positive and 69 negative with the other tests; the corresponding figures for MCFT were 119 and 52. It is claimed that the test can be completed in 30 minutes with great economy of time, material and personnel.

T. E. Osmond

Ansari, N., Faghih, M. A., Hajian, A. & Bijan, H. Contribution à l'étude de "Bejel" en Iran. Rapport préliminaire. [**Contribution to the Study of Bejel in Iran**] *Acta Med. Iranica.* 1957, Dec., v. 1, No. 4, 327–41, 9 figs.

It is well known that Bejel (endemic syphilis) is endemic in Iraq; in order to discover whether it was also found in that part of Iran which touches Iraq these authors carried out an investigation in Dacht-Michan on the river Karkheh 60 kilometres northwest of Ahwaz; this is shown on a map. The Arabs live in huts or tents along the rivers, the climate is temperate from December to April and hot for the rest of the year; water for all purposes is drawn from the streams and the inhabitants do little bathing in the colder weather; clothing is light in the hot weather and thicker in the cold. Infection is acquired through sexual contact, or contact of infants with parents, or through clothing or culinary utensils. 4 villages were the main subject of the enquiry, total inhabitants 1,450, number examined 325, number infected 89, percentage 117 [*sic*] [this should surely be 27].

Blood was examined by the VDRL test. The main clinical signs were generalized adenopathy, mucous patches, lesions of the skin and commisures, perianal region and bucco-pharynx; periostitis and mutilation of the bones were common in adults (these are shown fairly well in 8 figures). As regards age-groups the percentages of those affected were 2–5 years 33, 6–14 years 30, 15 and over 22. The commonest signs and symptoms in adults were old scars, mucous patches, cutaneous ulcers and hoarseness; in children aged 2–14 adenopathy, lesions of the angles of the lips, mucous patches, and hoarseness were the commonest; lists of these with their frequency are set out in 3 tables.

Children are more frequently infected than adults [or perhaps show evidence of infection more often] and the total incidence varies from 23 to 34%.

T. E. Osmond

Beerman, H., Nicholas, L., Schamberg, I. L. & Greenberg, M. S., with T. Guthe. **Syphilis Review of the Recent Literature, 1959–1960.** *Arch. Intern. Med.* 1961, Jan., v. 107, No. 1, 121–40. [103 refs.]

Merle, F. & Peuch-Lestrade, P. M. Gonococcie et stérilité au Cameroun. [**Gonorrhoea and Sterility in the Cameroons**] *Méd. Trop.* Marseilles. 1960, Nov.–Dec., v. 20, No. 6, 735–41, 1 map.

The authors investigated the various causes of sterility in the Cameroons, a map of which is shown in a figure. A list of 14 departments is given showing that 1,566 sterile women were examined; in 147 (9·38%) sterility was due to syphilis, in 670 (42·78%) to gonorrhoea, in 195 (12·45%) to other infection causes, in 294 (18·77%) to anatomical conditions, in 124 (7·91%) to hormonal imbalance and in 130 (8·68%) to other causes. In 50 patients carefully examined in hospital anatomical and

hormonal factors, syphilis and the RH factor seemed of little importance whereas 88% showed tubular obstruction; among these only one showed gonococci but the gono-reaction [complement-fixation] was positive in 52%. Of 181 sera examined by this reaction 33% were positive and of 126 examined for syphilis 12% were positive. In another hospital inflammatory causes were found responsible for 70% of cases of sterility most of which were considered due to gonorrhoea. Whether the sterility described above can account for the decrease in population in these areas is not altogether clear but it does show that the problem of gonorrhoea is a serious one.

[It seems remarkable that gonococci were only found in one case; reliance on the gono-reaction appears to have been over-stressed since few people put much faith in it nowadays.] *T. E. Osmond*

i. Fan, P. C., Hsu, J., Ma, J. T. & Liu, J. C. **Incidence of *Trichomonas vaginalis* in Chinese Women.** Reprinted from *Chinese Med. J.* Taipei. 1958, Dec., v. 5, No. 4, 169–81. [63 refs.]

ii. ——, ——, —— & ——. ***Trichomonas vaginalis* in Northern Taiwan.** Reprinted from *Nat. Defense Med. Center Selected Papers.* Taipei. 1958, 54–9. [18 refs.]

i. The results of this investigation are much the same as of the previous one [see above]; the patients mostly came from Taipei. A total of 1,184 women between 16 and 60 years fell into 4 groups and gave the following positive results: (1) 286 prostitutes, 54 positives (18·88%); (2) 282 unselected women with obstetrical or gynaecological conditions, 46 (16·31%); (3) 506 selected women with discharge 68 (13·44%); (4) 110 unselected normal women refugees 1 (0·9%); only the urine of these last was examined. The overall percentage was 14·27.

Vaginal specimens yielded 20·62% and urine specimens 3·75% positives. As regards age, in prostitutes the highest figures were in those aged 16–20 years (20·21%), in those attending gynaecological departments the highest were in the 41–50 year group (30·56%) and in the total 21·73% in the same group. Non-pregnant women gave a higher percentage (19%) than pregnant women (15%).

Results are set out in 5 tables.

This article includes the reported results of other investigations, a list of numerous countries with results obtained in them, an account of the organism and a comparison with other similar ones and a discussion of the pathogenicity or otherwise of the organism.

ii. This paper is based on the same material. *T. E. Osmond*

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

Levi, M. I., Basova, N. N. & Suchkov, J. G. **Optimal Conditions for Complement Fixation Reactions in Some Infections.** *Acta Virologica.* Prague. 1960, Nov., v. 4, No. 6, 348–55, 2 figs. [11 refs.]

This paper is concerned with complement-fixation reactions in various virus infections (lymphocytic choriomeningitis, influenza, ornithosis, tick-borne encephalitis), rickettsial infections (epidemic typhus, murine typhus, North Asian tick-borne typhus and Q fever) and bacterial infections (plague and brucellosis). The method of preparing the antigens and the immune sera used in the tests are described. The tests were set up by the "box" or "chequer-board" method and fixation temperatures and times ranged from 4°C. for 20 hours to 37°C. for 2 hours.

The highest dilution of antigen or immune serum showing complete absence of haemolysis at one hour after complete lysis of the red cells in the controls was taken as the limiting titre. The limiting titre of antigen determined at 4°C. for 20 hours was taken as 1 antigen unit (AU) and for the immune serum, determined under the same conditions, 1 antibody unit (SU). The index of efficiency for a given temperature and time of fixation was obtained from the arithmetical mean of the scores designating the degree of inhibition of haemolysis (4–0). Thus the total scores divided by the number in the "box" gave the index and the highest index in any series of CFT for a particular infection indicated the optimal time and temperature for fixation. *H. J. Bensted*

Haneveld, G. T. **Some Epidemiological Aspects of "Travellers' Diarrhoea" in Lebanon.** *Trop. & Geograph. Med.* Amsterdam. 1960, Dec., v. 12, No. 4, 339–44. [13 refs.]

"Travellers' Diarrhoea" [this *Bulletin*, 1960, v. 35, 264] has a global prevalence and has been given many names some of which are stated here. These common diarrhoeas produce only a slight indisposition in the ordinary tourist but may have more serious consequences for special groups as in the second world war in the Middle Eastern Theatre when "British troops were attacked in such a way that a military campaign could not successfully be conducted during the first weeks after arrival" [see also *Trop. Dis. Bull.*, 1944, v. 41, 606].

The observations of the author were made on the incidence of the disease in the observers recruited from 20 different nations of the United Nations Mission to Lebanon in 1958. A table which sets out the incidence

by country of origin shows 136 sufferers among 346 observers from Europe, 8 among 100 from Asia, 30 among 70 from Canada and 8 among 60 from South America.

There is some discussion of these national differences in immunity with reference also to the tendency for the incidence of diarrhoea to be higher in the lower age-groups and also that officers are more prone to attack than non-commissioned and lower ranks.

The aetiology of travellers' diarrhoea is also considered from the viewpoint of these observations and those recorded in the literature with the statement of opinion that "pure epidemiological considerations urge us to include the virus infections as a possible cause of this harmless but annoying disturbance".

M. E. Delafield

MEDALIE, M. **Antimicrobial Drugs in Lung Infections. A Comparative Study of Penicillin, Sulphonamides, Achromycin, Erythromycin, Chloromycetin and Albamycin T.** *Med. Proc.* Johannesburg. 1960, Dec. 3, v. 6, No. 24, 571–4, 1 fig.

A somewhat crude comparison was made of the effects of various drugs in bacterial infections of the lung (pneumonia, bronchopneumonia and bronchitis) in non-European children admitted to Boksburg hospital, Johannesburg. The main investigation was during the period May 1959 to April 1960, and the average age of the children treated varied from 1·4 to 4·2 years in the different groups. The dosage of each drug was predetermined on a uniform system based on body weight. The diagnosis seems to have been based almost exclusively on a chest radiograph, but some throat cultures, haemaglobin estimations, white blood counts, and sedimentation rates were also done. The clinical response, X-ray and blood findings seemed to indicate bacterial infection in nearly all cases.

Conclusions as to the effect of the drugs were mainly based on the average period of temperature elevation; this varied from 2 to 4 days approximately. Both penicillin and sulphonamides proved to be as satisfactory as the other drugs, and results were as good with long-acting sulphonamide and oral penicillin as with other forms of the drugs. It is concluded that nearly all these patients could have been treated as out-patients without detriment. The deaths in the series are summarily dismissed as irrelevant, because the majority of deaths in non-European child patients are the result of malnutrition; this is said to be "an economic rather than a medical problem".

H. Stanley Banks

SMITH, H. L. & ETTELDORF, J. N. **Parenteral Fluid Regimens in the Treatment of Severe Diarrhea in Infants.** *J. Pediatrics.* St. Louis. 1961, Jan., v. 58, No. 1, 1–16. [44 refs.]

This extremely detailed paper compares 3 methods of correcting fluid and electrolyte imbalance resulting from acute gastro-enteritis in infancy. In broad outline the modified Hartmann's method employed comprised infusion of a mixture of one-sixth molar sodium racemic lactate with hypotonic Ringer's solution, combined with the oral administration of dextrose, Amigen and a mixture of salts approximating to that present in breast milk. Darrow's method utilized one-half normal glucose saline as the initial rehydrating agent, followed by blood or plasma in severe cases. When renal flow was re-established, Darrow's potassium lactate solution was given subcutaneously and glucose solution intravenously. The amounts of infused fluid required when either of the above methods was used was calculated on a basis of body weight.

The Butler-Talbot method differs from the other two in that infusion fluid requirements are calculated from the patient's surface area. A hypotonic glucose saline solution is used to correct the fluid balance, after which a hypotonic multiple electrolyte solution is used to correct imbalance of those substances.

By each method a child of standard weight and surface area would receive a fluid of similar overall osmolarity, though the Butler-Talbot regime supplied most carbohydrate. Most sodium is supplied by the modified Hartmann method and least by that of Butler-Talbot. Most potassium is supplied by the Butler-Talbot regime and least by the modified Hartmann, and in chloride content the 3 systems show the same declining order of precedence.

The results of each regime in 3 groups of infants numbering 53 in all are tabulated in great detail and cannot be abstracted. Under the modified Hartmann system, while acidosis was relieved very promptly, there was a strong tendency for alkalosis, hypernatraemia and hypokalaemia to result. This has led the authors to modify further the salt mixture for oral use and to substitute one-twelfth for one-sixth molar sodium racemic lactate solute. The Butler-Talbot regime, while restoring potassium depletion adequately, only slowly corrected the acidosis; hyperkalaemia sometimes developed but did not give rise to symptoms. Darrow's method rapidly restored the fluid balance and the levels of sodium and potassium in the blood, but was slower than the Hartmann, though faster than the Butler-Talbot system, in restoring a normal acid-base equilibrium.

[At this stage the abstracter, his brain paralysed by the complexity of this paper, feels compelled to put down his pen and to exhort all those with a special interest in this subject to consult the paper in its original form.]

J. H. Walters

PONTECORVO, M. Vaccinazione associata contro la difterite, la pertosse, il tetano e la poliomielite. **[Combined Inoculation against Diphtheria, Pertussis, Tetanus and Poliomyelitis]** *Riv. Istituto Sieroterap. Ital.* 1960, Nov.–Dec., v. 35, No. 6, 661–78. [46 refs.] English summary.

The value and methods of administration of prophylactic inoculations for diphtheria, pertussis, tetanus and poliomyelitis are discussed with special reference to interference effects where mixed inocula are used and to the timing of their administration. It is submitted that in Italy the commencing age should be 4 months. The reasons for this are (a) that statistics show a higher incidence of poliomyelitis in the first year of life in

Italy than in other countries; (b) that antigen is less effective when a considerable amount of antibody carried over from the mother is still present in the infant. At 4 months the passively acquired poliomyelitis antibody has usually fallen sufficiently to permit of good response to the vaccine.

In discussing the problem of the possible influence of the associated prophylactics on the development of poliomyelitis, attention is drawn to the association of pertussis vaccine with the rare cases in which poliomyelitis appears as a sequel to inoculation. It is further suggested that such results have been more often associated with bacterial suspensions killed with merthiolate [thiomersalate] than with those killed with formaldehyde, the former being less effectively detoxicated and therefore more deleterious to the nervous system [this *Bulletin*, 1960, v. 35, 1110]. *J. W. McLeod*

J. Pediatrics. St. Louis. 1961, Feb., v. 58, No. 2, 149–94, 5 figs. [Numerous refs.] **Symposium on the Chemoprophylaxis of Infection.**

According to R. G. Petersdorf, *Introduction and general principles* pp. 149–52, three-fourths of all antibiotics are given to *prevent* rather than to *treat* infections. The neonate is given an antibiotic to prevent ophthalmia, another to avoid staphylococcal infection from a breast abscess and further doses to protect it against the "bacterial complications" of measles, chickenpox and the common cold. At school he may be given an antibiotic against streptococcal, meningococcal or intestinal infection and in later life in order to avoid the complications of respiratory disease, post-operative sepsis, infections supervening on cardiac, chest or kidney disease or the bacterial hazards of in-dwelling catheters, tracheostomy tubes or sutures. Yet the evidence for the efficacy of these practices has rarely been scrutinized. The author suggests that aimed at one specific pathogen, antibiotic prophylaxis can be highly successful—*e.g.* against streptococcal relapses in rheumatic subjects—but when used as an umbrella to cover infection-prone patients it may result in resistant flora being established—the umbrella usually leaks. Antibiotics have 3 disadvantages—toxic and allergic reactions, superinfection, and expense.

In the second article, *The use of antibiotics to prevent infections by specific pathogenes* pp. 153–63 R. G. Petersdorf and T. E. Woodward refer to experimental work in scrub typhus, Q fever and tularaemia. Volunteers were inoculated with the responsible organism and given antibiotics at varying intervals thereafter. Volunteers inoculated with *Rickettsia orientalis* and given 1·0 gm. of chloramphenicol daily for 28 days from the day of infection developed the disease 5 days after the drug was stopped. If prophylaxis was withheld for 7 days after infection and chloramphenicol then given in single doses at 4-day intervals the outcome depended on the dose: 3·0 gm. doses led to suppression of clinical symptoms though rickettsaemia still occurred, but with 2·0 gm. doses the disease became manifest. Treatment with chloramphenicol on the first day of illness was followed by a dramatic response but relapses were frequent: if treatment was withheld till the 5th day, relapses did not occur.

In Q fever, treatment with terramycin [oxytetracycline] in the first 24 hours of infection leads to rapid cure and relapses are rare. Volunteers inoculated with *R. burneti* and given the drug late in the incubation period did not develop the disease but those given it within 24 hours of infection developed the disease when the drug was stopped. Volunteers infected with *Brucella tularensis* and given streptomycin within 1 hour of infection for 5 days did not develop the disease: those given chloramphenicol developed the disease when the drug was stopped. It is clear that a drug given prophylactically in the incubation period may not prevent disease but simply prolong the incubation period unless the drug is bactericidal. It also appears that the time intervals between infection and prophylaxis and between the onset of illness and treatment affect the development of immunity and the occurrence of overt signs or of relapse: but it is clear that these factors appear to operate differently in different diseases. In contrast to the difficulties with the intracellular parasites of scrub typhus, Q fever, etc., antimicrobials used against haemolytic streptococci, meningococci, gonococci, shigellae and sometimes staphylococci usually prevent clinical disease: it may be that in these instances immune mechanisms are less important.

The prevention of rheumatic fever relapses by antimicrobial prophylaxis is assessed critically by A. R. Feinstein, R. G. Petersdorf and Ann A. Browder in their article *Prophylaxis of post-streptococcal sequelae and bacterial endocarditis* pp. 164–73. Once-monthly injection of long-acting penicillin seems the most reliable method but its efficacy may be due to high serum levels for a few days following injection rather than to prolonged low levels: short courses of oral penicillin given once monthly might achieve the same effect. Sulphonamides are very satisfactory and the long-acting sulphonamides may prove especially useful. Acute haemorrhagic glomerulonephritis may occur after inapparent streptococcal infection but immunity to the responsible streptococcal types follows an attack and subsequent prophylaxis is unnecessary. Subacute bacterial endocarditis is only rarely caused by group A streptococci and further study is required on the best form of prophylaxis to cover dental operations, tonsillectomy, urethral and cardiac surgery in susceptible subjects.

The widespread use of antibiotics in maternity and neonatal wards has not resulted in a clear understanding of the part played by infection in the neonatal period. R. G. Petersdorf, Ann A. Browder and A. R. Feinstein, in their article *Protection against infection in susceptible individuals* pp. 174–194, refer to various controlled experiments, not all of which yielded evidence that routine prophylaxis was of value: they feel that definitive studies have yet to be performed. The use of antibiotics in non-bacterial upper respiratory diseases, in whooping cough, and in measles also rests on an insecure basis: and in severe poliomyelitis is of no value at all. Antibiotic prophylactic cover for surgical operations is almost universal but it is frequently not justified and sometimes based on wishful thinking rather than on scientific facts. In chronic bronchitis antibiotic therapy is of proved value though it is still not clear how the drugs may best be used. In all conditions the benefits to be derived from the drugs must be weighed against the hazards—mainly toxic effects and superinfection with

resistant organisms. [These 4 articles should be studied in the original: they deal in an unbiased manner with a subject which confronts physicians and surgeons every working day.] *A. B. Christie*

HOSPITAL AND OTHER CROSS INFECTIONS

WHITE, A. **Quantitative Studies of Nasal Carriers of Staphylococci among Hospitalized Patients.** *J. Clin. Investigation.* 1961, Jan., v. 40, No. 1, 23–30, 4 figs. [17 refs.]

In confirmation of previous work, staphylococci from lesions in patients in a general hospital in Louisville, Kentucky, were more frequently resistant to antibiotics than those from carrier sites. 64% of 100 lesion strains, and 26% of 2,134 carrier strains were found to be type 80, 81 or 80/81; 30% of the carrier strains, but only 8% of those from lesions were in phage group III. Carriers of type 80/81 strains tended to yield more staphylococci from their nasal cultures than carriers of other types. Persistent carriage was also associated with the larger numbers of staphylococci in the cultures. Sweep-plate cultures from the beds were positive in 40% of cases when the patients nose culture yielded 10^4 or more colonies, but in 20% or less when the nose yielded 10^3 or fewer. Treatment with penicillin or tetracycline had little effect on the total nasal carrier rate; erythromycin led to a slight reduction; all drugs tended to lead to an increased rate of carriage of hospital types of staphylococci.

[See also this *Bulletin*, 1959, v. 34, 491.]

R. E. O. Williams

BURKE, J. F. & CORRIGAN, E. A. **Staphylococcal Epidemiology on a Surgical Ward. Fluctuations in Ward Staphylococcal Content, its Effect on Hospitalized Patients and the Extent of Endemic Hospital Strains.** *New England J. of Med.* 1961, Feb. 16, v. 264, No. 7, 321–6, 4 figs.

The air and equipment of a surgical ward in the Massachusetts General Hospital was examined for staphylococci at frequent intervals over 6 months. The ward had 48 beds, 40 in 4-bed cubicles and 8 in single rooms. Particular phage types of staphylococci were found to appear and disappear at short intervals and strains were rarely present in one area for more than a few days. The average number of different strains found in the ward in a week was 16. In a more intensive study of a single 4-bed cubicle alternately housing a patient with or without a septic lesion, it was found that asymptomatic carriers rarely contaminated their environment, but that patients with an open staphylococcal lesion commonly dispersed their staphylococcus into the air of the room. Staphylococci did not persist long in the room after the patient left.

Of 320 ambulatory patients admitted to the ward no fewer than 79% carried coagulase-positive staphylococci in nose or throat or on the skin. 122 patients carried 83 different strains. 42% of 183 patients exchanged their staphylococcus, or acquired a new strain, during their stay in the ward, but there was no overall increase in the carrier rate. There was no evidence that the patients were discharged carrying "hospital" strains of staphylococci. Antibiotic treatment had no detectable effect on the carrier state of the patients.

[In the reviewer's experience some asymptomatic nasal carriers of staphylococci produce widespread contamination of their environment. The authors' finding that their patients' carrier state did not increase during their ward stay, and was unaffected by antibiotics, differs from other published experience. It is interesting to speculate on possible reasons for this difference; one may be the subdivision of the ward into 1- and 4-bed units.]

R. E. O. Williams

BACTERIAL INFECTIONS

The order in this section is:—***General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.***

DODIN, A., with the technical collaboration of J. RANDRIARINORO. La diphtérie à Madagascar depuis la fondation de l'Institut Pasteur (1898). **[Diphtheria in Madagascar since the Foundation of the Pasteur Institute]** *Arch. Inst. Pasteur de Madagascar.* 1960, v. 28, 35–45, 2 charts. [12 refs.]

In regard to diphtheria, Madagascar seems to be in a bad way; it is apparently becoming one of nature's "reserves" for the survival of the bacillus. Since 1947 the incidence has steadily increased among the indigenous population—up to 363 cases with 46 deaths in 1959. Among Europeans the disease is much rarer.

The main incidence is in children, particularly those of school age; the infection seems to be largely spread in the schools. Since 1931 the Pasteur Institute has produced material for immunization of only 45,000 persons. The cost of the 400-odd cases in 1959 is estimated at around 6 million francs, not counting the physical suffering, temporary and permanent incapacity for work, and the deaths. The obvious answer is to apply prophylactic immunization, especially to children of pre-school age. *H. Stanley Banks*

WHITAKER, Jo Anne, DONALDSON, P. & NELSON, J. D. **Diagnosis of Pertussis by the Fluorescent-Antibody Method.** *New England J. of Med.* 1960, Oct. 27, v. 263, No. 17, 850–51.

The globulin fraction of antiserum against *Bordatelle pertussis* was conjugated with fluorescein isothiocyanate and absorbed with organisms to which cross staining was observed. The final adsorbed antiserum caused bright fluorescent staining of pertussis organisms but no fluorescence of other pathogens tested. Pernasal

pharyngeal swab specimens were stained for 20 minutes with conjugated antiserum and examined for fluorescent organisms.

The test was shown to be rapid and specific, positive results were obtained in 94% of 96 patients with whooping-cough who had received no antibiotics, and who had been ill for less than 3 weeks. The incidence of positive fluorescent smears fell to 57% in patients who had a cough for over 3 weeks and to 11% in those who had received prior antibiotic therapy. *F. T. Perkins*

JOÓ, I., PUSZTAI, Susanna & JUHÁSZ, Vera P. **A Comparative Study of the Effectiveness of Different Standard *pertussis* Vaccines.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 4, 401–10. [24 refs.]

The English summary appended to the paper is as follows:—

"Standard pertussis vaccines prepared in this laboratory were compared by the active mouse protection method to standard vaccines from abroad.

"No significant difference was found between the American (USV), the British (BV) and the Hungarian (Hu V 1) standard vaccine preparations.

"Both Hu V 2 and Hu V 3 standards prepared in our laboratory appeared to be more effective (about one and a half times) than the USV, BV and Hu V 1 standard vaccines. The difference was not statistically significant.

"The protective value of the international standard vaccine (IV) was significantly higher than that of the other standard vaccines.

"No significant differences were found between the individual results of parallel determinations of the protective value of the same vaccine within the same experiment.

"Certain problems of the evaluation of the results obtained by active mouse protection test are discussed."

TAYLOR, Joan. **The Diarrhoeal Diseases in England and Wales with special reference to those caused by *Salmonella, Escherichia* and *Shigella*.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 6, 763–79, 2 figs. [Numerous refs.]

[The broad bacteriological pattern of the diarrhoeal diseases as seen in England and Wales is not fundamentally different from that found in other economically advanced countries—in so far as the *Salmonella, Shigella* and *Escherichia coli* are concerned. The enteropathogenic *coli* are the most frequently associated with the diarrhoeas of infants although *Shigella* and *Salmonella* are often involved. In older children *Sh. sonnei* is the most important organism whereas in adults the condition may be due to Sonne dysentery introduced into a family by one of the younger members or to a salmonella infection due to a particular serotype contaminating an article of food. This is the very broad picture which is common in most of the advanced countries of the world at the present time. The diarrhoeal diseases of infants and young children are of special importance in world studies because the pattern they present in different countries largely reflects the economic state and public health conditions in each case. In backward countries there is usually a good deal of poverty, malnutrition, low standards of hygiene, etc., with a high infant mortality mainly due to diarrhoeal diseases. The organisms predominantly responsible for these diseases in, for instance, Senegal [BAYLET, this *Bulletin*, 1960, v. 35, 577] are Shiga and Flexner dysentery—common causes of the adult dysentery in the area. The enteropathogenic *coli* and *Sh. sonnei* are rarely isolated. Another striking difference is seen in the isolation-rate of pathogens from the stools of infants with acute diarrhoea. In highly advanced countries like Great Britain, in spite of the recognized importance of *E. coli* in infant diarrhoea, the overall isolation-rate of the enteropathogenic *coli*, *Sh. sonnei* and salmonellae is comparatively low and in a high proportion of cases no bacterial cause can be found, yet in the Senegal survey Shiga or Flexner bacilli appear to have been isolated from a large proportion of the African patients.]

Dr. Taylor's account of the diarrhoeal diseases in England and Wales gives a much more detailed picture of the bacteriology of neonatal diarrhoea and discusses the individual serotypes of *E. coli* at some length. She also considers salmonella infections in England and Wales in relation to the salmonella-contamination of home produced and imported foods and feeding-stuffs and shows how a particular serotype can be identified with a certain article coming from a particular country. The article contains a great deal of valuable information and is full of interest.

During the last few years the literature on diarrhoeal diseases has grown enormously and increasing attention has been paid to the enteropathogenic *coli* in relation to neonatal diarrhoea but the aetiology of the disease is still far from being understood.

This paper forms a useful companion to the symposium which appeared in the WHO *Bulletin* in 1959 [*ibid.*, 1960, v. 35, 668] and should be read in conjunction with it by those interested in the diarrhoeal diseases as a world problem. *H. J. Bensted*

DUMAS, A., FOLEY, A. R. & BRETON, J. P. **A Milk-Borne Epidemic of Typhoid Fever in Montmagny, Quebec, 1959.** *Canadian J. Pub. Health.* 1961, Feb., v. 52, No. 2, 68–71.

In March 1959 a serious typhoid epidemic of 197 reported cases occurred in Montmagny, Quebec, a town with a population of 6,000. No cases of typhoid fever had occurred in the area during the previous 2 years but before that 1 or 2 cases had usually been reported each year always among residents on the banks of the Rivière-du-Sud which is a polluted stream.

This typhoid epidemic began with the reporting of 8 probable cases of typhoid infection in the Montmagny hospital, reached its peak in mid-March with 41 cases in a week when epidemiological investigation was begun and then gradually diminished though occasional cases were reported up till mid-June.

The story of the investigation is well told. It led ultimately to the incrimination of the raw milk supplied by 1 of the 4 dairymen who served the people of the area. This dairyman had always used water from his

private well for dairy purposes until this well had dried up over a month previously and he had then used the river water without boiling it as a family supply and for cleaning the dairy equipment. He had added chlorine to the water employed for cleaning the utensils which were left to dry but before being used were rinsed with the unchlorinated polluted water.

Typhoid fever occurred in 105 families and the distribution of the disease ranged from 1 case in each of 65 families to the maximum of 8 cases in 1 family which was that of the dairyman himself! The age distribution is stated and incidence was greatest in the lower age-groups—69 in the 0–9-year, 54 in the 10–19-year and 28 in the 20–29-year group.

Treatment of the patients was by chloramphenicol and there were no deaths. The invading organism in all cases was phage type E1.

Measures taken for control of spread of the infection are stated. *M. E. Delafield*

SEIDLER, L. Klinischer Beitrag zur Pathogenese des Relapses beim Bauchtyphus. **[The Pathogenesis of Relapses in Enteric Fever]** *Ztschr. f. ärztl. Fortbildung.* 1961, Jan. 1, v. 55, No. 1, 15–18.

The study described in this paper was undertaken to throw light on the question of whether the treatment of enteric fever with chloramphenicol influences in any way the occurrence of relapses.

A comparison was made between the recorded relapse rates observed in patients in the periods 1947–49, 1950–51 and 1952–58. In the first period 546 patients treated only symptomatically had 31 (5·6%) relapses; in 1950–51 on inadequate chloramphenicol treatment there were 32 (10·1%) relapses in 315 patients but in the third period when full chloramphenicol treatment had become possible the relapses in 636 patients numbered 43 (6·7%) a percentage not significantly different from that of the first period. A precise analysis of the case histories in the second period showed that a proportion of the 10·1% of the recorded relapses were not true relapses but only an interruption in the expected temperature curve. These observations and others on the possible causation of relapses lead to the conclusions: (1) chloramphenicol treatment influences neither the occurrence of relapses nor their absence, (2) inadequate chloramphenicol treatment does not bring about a true relapse, (3) no evidence was found that relapses may result through interrupted bed rest, errors in diet or the use of the duodenal sound, and (4) in a number of cases specially investigated it was found that the relapse was caused by the original phage type and not by superinfection by a different type.

M. E. Delafield

PRZEGLĄD EPIDEMIOL. Warsaw. 1960, v. 14, No. 3, 193–382, illustrated. [Numerous refs.] English summaries. Pamietnik i zjazdu naukowego Polskiego towarzystwa epidemiologów i lekarzy chorób zakaznych. Warszawa 20–21 listopad 1959. Temat drugi: Czerwonka bakteryjna. **[Memoirs of the Ist Congress of the Association of Polish Epidemiologists and Infectionists. Warsaw, November 20–21, 1959. Second Problem: Bacillary Dysentery]**

The papers presented at the First Congress of the Polish Association of Epidemiologists and Infectious Diseases Physicians which are now published occupy an entire number of the journal and are devoted to various aspects of bacillary dysentery in Poland.

Four main addresses were given, in which the aetiology, epidemiology, clinical aspects and treatment of bacillary dysentery were reviewed, with particular reference to the disease in children. Analysis of the incidence of dysentery in Krakow between 1887 and 1957, and in Poland and adjacent countries between 1919 and 1957, showed that the disease occurs in cycles, each lasting 20–30 years, which are associated with changes in the predominant species of *Shigella*. The clinical course was analysed in 150 patients suffering from acute and 25 from chronic dysentery, and the relationship between the frequency of the different symptoms and the species of *Shigella* isolated from the patient was investigated. The standard therapeutic measures are employed for the treatment of dysentery in Poland, and great importance is attached to the system of out-patient's clinics for enteric infections, where convalescents can attend after discharge from hospital and receive treatment designed to prevent relapses and the development of the carrier state.

Apart from the main addresses, 26 short papers were presented at the Congress which contain much miscellaneous information on the situation with regard to dysentery in Poland. In the examination of 11,933 strains of dysentery bacilli isolated from patients and carriers in 10 provinces of Poland in 1955–57 *Shigella flexneri 2a* was found in 31·0–40·9%, other sub-types of *Sh. flexneri* in 21·6–28·5% and *Sh. sonnei* in 28·0–44·4% of cases; *Sh. flexneri 2a* was commoner in patients, and *Sh. sonnei* in carriers. Among 830 strains isolated in the town and province of Wrocław in 1955–58 541 (65·2%) were *Sh. flexneri* and 289 (34·4%) were *Sh. sonnei*. The results of phage-typing of 1600 strains of *Sh. sonnei* isolated in all parts of Poland in 1955–58 showed that 36 types were present in the country, the commonest being type 2 (27·6%) and type 3 (31·2%), followed by type 7 (11·35%) and type 6 (9·56%). The commonest biochemical types were type a (50·6%), type b (17·3%) and type k (15·3%). A new type was encountered (type m; 77 strains, 5·1%), which did not ferment maltose. Phages isolated from the faeces of patients have also been used for typing *Sh. flexneri*. The value of sigmoidoscopy in the confirmation of the diagnosis of dysentery is discussed; in a group of 251 patients suffering from dysentery between 1955 and 1958 the diagnosis could be confirmed bacteriologically in 95, whereas on sigmoidoscopy characteristic lesions were seen in 208 patients. Chronic dysentery in Poland is caused more frequently by *Sh. flexneri* than by *Sh. sonnei* or *Sh. flexneri 6* (var *newcastle*); of 40,000 apparently healthy persons 0·9% were found to be carriers; 144 of 207 carriers investigated had no previous history of any illness resembling dysentery. An outbreak of dysentery in a young persons' institute in Poznan which took the form of food poisoning is described, 47 cases occurred over a period of 5 days among 65 inmates (and an unstated number of staff) at risk. The food was infected from the hands of a cook who was suffering from mild dysentery. *Sh. flexneri 2a* was identified as the cause of the outbreak. The value of various methods of establishing a diagnosis of dysentery was examined in

a group of 860 patients observed in Gdansk between 1952 and 1957. A typical clinical picture was the most frequently occurring criterion, followed by the results of bacteriological investigation and sigmoidoscopy, with serological results coming last.

In the remaining papers the sigmoidoscopic appearances in acute and chronic dysentery are described, together with their value as a diagnostic measure, and also the haematological aspects of dysentery and a number of miscellaneous topics. The symposium closes with several pages of discussion. *D. J. Bauer*

SAVIC, S. Epidemija dizenterije u bolnici u Pirotu. **[Epidemic of Dysentery in the Pirot Hospital]** *Higijena.* Belgrade. 1960, v. 12, Nos. 2/3, 274–82, 1 graph & 1 plan.

In November and December 1956 an epidemic of bacillary dysentery occurred in the hospital in Pirot, Yugoslavia, with a total of 51 cases, including 27 among the staff [the total number of persons at risk is not stated]. The course of the illness was mild in 27 (52·9%), moderate in 17 (33·3%) and severe in 7 patients (13·8%). The diagnosis was established bacteriologically in 27 patients (52·9%) by the isolation of *Shigella flexneri 2a* and *Sh. schmitzii* [*Sh. dysenteriae 2*]. The infection was derived from a carrier and was spread by contact, food and water. *D. J. Bauer*

DRACHMAN, R. H., PAYNE, F. J., JENKINS, A. A., MACKEL, D. C., PETERSEN, N. J. BORING, J. R., GAREAU, Florence E., FRASER, R. S. & MYERS, G. G. **An Outbreak of Water-Borne *Shigella* Gastroenteritis.** *Amer. J. Hyg.* 1960, Nov., v. 72, No. 3, 321–34, 4 figs. [30 refs.]

The outbreak described in this paper occurred in a small township in Utah with a community of some 1,600 people, and appears to have been due to an inadequate water supply to the town in summertime being augmented by water from a polluted irrigation canal without proper safeguards. The outbreak was explosive and involved almost one-third of the population at risk. Although this epidemic is classified as a *Shigella* gastroenteritis it was by no means typical as judged by the experience of other outbreaks ascribed to this cause. The organism incriminated was *Shigella flexneri 6* of the Manchester variety, which however was isolated from only 16% of 218 of the persons examined bacteriologically (but from 32% of 78 of them who were affected) and the clinical picture was more in keeping with gastroenteritis than bacillary dysentery. The canal water was highly polluted with *Escherichia coli*, and *Sh. flexneri 6* was not isolated from any of the speciments examined. The illnesses in those affected were mild, of short duration and in the main quite unlike the picture usually seen in outbreaks of shigella infections. From the account presented in this paper it would seem that the outbreak was predominantly due to the consumption of water highly polluted with *E. coli* and that the role played by *Sh. flexneri 6* was secondary. The evidence, however, is incomplete and it is not possible to say with any degree of certainty what was the primary bacterial cause of the outbreak. *H. J. Bensted*

KOVALEVSKAIA, I. L. **The Use of Alcohol Dysentery Vaccine over 10 Years.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 4, 709–16, 1 fig. [32 refs.] [Translated from Russian.]

This is an uncritical assessment of the value of Shiga-Flexner alcoholized vaccines in the treatment and prevention of bacillary dysentery and appears to be based mainly on the selected reports of other workers. It is stated that alcohol dysentery vaccines were introduced in the U.S.S.R. in 1943 and have proved to be of great value in the treatment of chronic dysentery. There is no information about the preparation of this particular form of vaccine or about its essential difference from other dysentery vaccines; it is merely stated that the effectiveness of the alcohol vaccine was 2·7–6 times higher than the oral vaccine which gave results of the same order as those pentavalent and polyvalent vaccines from other sources. *H. J. Bensted*

YAMADA, C. **An Evaluation of *Shigella* Vaccines by Hemagglutination on Human Sera from Vaccinated Volunteers.** *Japanese J. Med. Sci. & Biol.* 1960, June, v. 13, No. 3, 77–90. [15 refs.]

In attempting to assess the value of *Shigella* vaccines for the prevention of bacillary dysentery many workers have found that although bacterial agglutinins for *Sh. flexneri* can be demonstrated in the sera of volunteers receiving a polyvalent vaccine those for *Sh. sonnei* cannot be detected. Nevertheless the much more sensitive haemagglutination test showed that measurable haemagglutinins developed in both immunized subjects and also in patients suffering from Sonne dysentery.

The present paper is concerned mainly with the haemagglutinin response to Sonne antigens in vaccinated subjects and also to natural infections with *Sh. sonnei*. Low haemagglutinin titres were found in unimmunized normal subjects both for *Sh. flexneri* and *Sh. sonnei* and after vaccination these were significantly increased and persisted for about a year. Patients convalescent from bacillary dysentery showed haemagglutinin titres of 1:160 or more, the levels being perhaps a little higher than attained after vaccination even with booster doses. There was little evidence to suggest that *Sh. sonnei* vaccines in field trials were effective in protecting against the disease and the author concludes that, if high antibody level in the serum offers protection against bacillary dysentery, vaccine prophylaxis does not provoke a good enough antibody response to be regarded as having any such effect. *H. J. Bensted*

URMENYI, A. M. C. & FRANKLIN, A. W. **Neonatal Death from Pigmented Coliform Infection.** *Lancet.* 1961, Feb. 11, 313–15. [12 refs.]

Pigmented organisms belonging to the *Cloaca* group A were isolated from the brains of 2 infants dying within 2 days of each other in St. Albans City Hospital: the organisms were isolated also from the cerebrospinal fluid and bronchus in one infant, and from the bronchus, liver and marrow in the other. Both infants had made normal progress after birth, one for 10 days, the other

for 5 before developing the rapidly fatal infection. The infants had not been in contact with each other except that an incubator used for the first child may have been used for the second child also a week later. Bacteriological tests failed to find any pathogenic organisms in the incubator but showed that the inhalation of aerosol infection was a possibility. One of the infants was a twin but the other twin showed no evidence of infection.

A. B. Christie

UJVÁRY, G. & PÁLL, G. **Studies on the Incidence of *E. coli* Serotype O:125 B:15 (var. *canioni*).** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 4, 341–9, 2 figs.

The English summary appended to the paper is as follows:—

"During a hospital epidemic the rare enteropathogenic strain *E. coli* O:125 B:15 was isolated in 52 cases out of faecal samples collected from 1033 sick infants and children. The morphology, biochemical activity, serology and antibiotic sensitivity of the strains isolated was examined. Out of the 52 patients 30 had enteral symptoms. Symptoms were mild in 18, medium in 9 and severe in 3 cases. Twenty-two patients had no enteral symptoms. Attention is drawn to the importance of the resistance being decreased by extraenteral pathologic processes, particularly influenza and its complications. The therapy applied and the environmental factors possibly playing a role in the spreading and development of the epidemic are discussed. On the basis of the findings we regard type O:125 B:15 of *E. coli* as a facultative enteral pathogenic agent in infants."

PERGER, F. Colifloral, vermehrungsfähige Coli-Bakterien in Tablettenform. **[Colifloral, *Escherichia coli* capable of Reproduction Administered as Tablets]** *Wien. med. Woch.* 1960, Oct. 1, v. 110, No. 39, 804–8, 3 figs. [17 refs.]

Colifloral is a preparation which is made up in the Serotherapeutic Institute of Vienna. It consists of 2½ thousand million *Escherichia coli* of mixed strains which are lyophilized and incorporated with suitable nutrient medium and a synthetic cellulose in the form of tablets. Observation with such tablets containing also barium salts show that the liberation of the bacteria takes place in the lower ileum and in the large intestine. It is claimed that this is a more successful method of implanting normal *E. coli* on an intestine carrying an unusual flora, such as *proteus* and paracolon bacteria, than any other up till now adopted.

Such replacement, it is claimed, is often successful in the treatment (a) of the disorders of bowel function which commonly follow administration of antibiotics; (b) certain rheumatic conditions associated with the presence of an unusual bowel flora—presence of *Dysbakterie* as the author describes it; and (c) some of the lesser phases of mental failure such as mild melancholia.

In respect to (b) and (c) the author appears to be presenting interesting speculations rather than conclusions supported by a great weight of evidence.

J. W. McLeod

POBEREZKIN, M. N. **Features of the Course of Brucellosis in Vaccinated Persons.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 2, 305–10. [Translated from Russian.]

This is a report of a field trial of dry living vaccine against brucellosis, which extended over the period 1950–1957 and involved some 63,000 persons being vaccinated. It is not stated how many persons in the trial were unvaccinated or how the trial was controlled or assessed. The overall figures showed that the incidence of brucellosis among the vaccinated persons was 0·05% as against 1·3% for the unvaccinated. In foci of goat-sheep brucellosis involving 13,614 vaccinated persons the percentage incidence of brucellosis among the vaccinated was 0·2 against 2·6 for the unvaccinated. The incubation period of brucellosis in the vaccinated was longer, the clinical course of the disease was milder and shorter and relapses were fewer than in the unvaccinated persons. The effect of vaccination was maximal up to the 6th month after the administration of the vaccine.

H. J. Bensted

KASYMOVA, K. A., BEKLEMISHEV, N. D. & UZBEKOVA, B. R. **Vaccination against Brucellosis of Persons with Positive Immunological Reactions.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 4, 643–50. [Translated from Russian.]

The vaccine used in this study was a dried live culture of *Brucella abortus*, Strain 19, which was reconstituted in a concentrated form so that 2 drops contained about $5{,}000 \times 10^6$ organisms. The two drops were placed separately on the surface of the skin of the upper arm and scarification made through the drops as in smallpox vaccination with cross hatching.

Persons giving a positive brucellin reaction (or presumably a positive serological reaction) who were without any history of an active brucella infection did not show any serious reaction after percutaneous vaccination with the living vaccine although both general and local reactions were observed in about 50% of these cases. Those, however, with a definite history of brucellosis with typical clinical manifestations reacted very strongly with raised temperatures and a clinical illness.

H. J. Bensted

DITCHFIELD, J., MEADS, E. B. & JULIAN, R. J. **Tularemia of Muskrats in Eastern Ontario.** *Canadian J. Pub. Health.* 1960, Dec., v. 51, No. 12, 474–8, 2 figs. [18 refs.]

"(1) Tularemia was discovered among the muskrat (*Ondatra zibethica*) in the Castor swamp, approximately 35 miles south-west of Ottawa.

"(2) *Pasteurella tularensis* was recovered by a Millipore filter technique from 3 out of 22 water samples collected from streams draining the swamp.

"(3) *Pasteurella tularensis* was also recovered from pools of the rabbit tick (*H. leporis—palustris*) collected in the area.

"(4) Most of the common vectors for transmission of the disease from animals to man are present in the Castor swamp region."

GWEE, A. L. & NADARAJAH, I. **A Survey of Tetanus in Singapore.** *Singapore Med. J.* 1960, Dec., v. 1, No. 4, 164–6.

In reviewing the incidence and mortality from tetanus in Singapore in the years 1957–59, the authors found that mortality had increased both in the neonatal and older groups. They felt that increases in the virulence of the organism and in the susceptibility of the population were unlikely explanations and thought it possible that the more aggressive therapeutic attitude of recent years resulting in more heroic treatment was having an "adverse result on the recovery chances".

A. B. Christie

PATEL, J. C., MEHTA, B. C., DHIRAWANI, M. K. & MEHTA, V. R. **Relapse and Recurrence of Tetanus.** *J. Ass. Physicians India.* 1961, Jan., v. 9, No. 1, 1–5. [11 refs.]

From November 1954 to October 1958, 2,007 cases of tetanus were admitted to the K.E.M. Hospital, Bombay; 17 recurred after cure: 4 of these second attacks occurred within 6 months of the first attack and were regarded as relapses, and 13 occurred after 6 months and were regarded as reinfections. The incidence of recurrence in the series was 0·847%. The authors feel that second attacks may be due either to overwhelming infection with a virulent organism or to the failure of immunity to develop after the first attack. They recommend active immunization of patients who recover from an attack of tetanus and the administration of toxoid-antitoxin to immunized persons sustaining an injury.

A. B. Christie

ALSTON, J. M. **Recent Developments in Leptospirosis.** *Proc. Roy. Soc. Med.* 1961, Jan., v. 54, No. 1, 61–7 (Sect. Comp. Med. 1–7). [43 refs.]

It is quite impossible to abstract this excellent review which medical and veterinary workers should find interesting and useful. The subject is dealt with under the following headings: morphology, colonial growth of leptospires in solid medium, metabolism, serotypes and their origin, pathogenicity, leptospiral disease of domestic animals, leptospiral disease of man, treatment, and prevention.

Over the past 15 years or so it has been realized that leptospirosis is one of the more important zoonoses with a very wide geographical distribution. The author has already produced a standard book on the subject in collaboration with the late Dr. J. C. BROOM [this *Bulletin*, 1958, v. 33, 899]; the present review is an admirable post-script to this work.

L. H. Turner

KOLOCHINE-ERBER, B. & MAILLOUX, M. Les leptospiroses humaines à *L. pomona* et *L. mitis* Johnson 1942 (maladie des porchers). **[Human Leptospirosis induced by *L. pomona* and *L. mitis* Johnson 1942 (Swineherd's Disease)]** *Ann. Inst. Pasteur.* 1961, Jan., v. 100, No. 1, 53–70, 2 figs. [71 refs.]

"Swineherd's Disease", often caused by *Leptospira pomona*, is clinically benign. BOUCHET, in 1914, was the first to note the association between a clinical syndrome in human beings (*pseudo typhoméningite*) and an occupational contact with pigs. GSELL [this *Bulletin*, 1944, v. 19, 768; 1946, v. 21, 373; 1947, v. 22, 325] was the first to show that *L. pomona* was the aetiological agent of swineherd's disease and now it is known that the distribution of this serotype is practically world-wide. DURAND *et al.* [*ibid.*, 1937, v. 12, 210; 1938, v. 13, 127, 128] in fruitless attempts to demonstrate the cause of the disease by animal experiments, collected tissue and sera. One of the authors was given some of these specimens in 1949: leptospires could not be detected in the tissues, which may have deteriorated, but 4 out of 14 of the sera agglutinated *L. pomona* to titres of 1:1000–1:10,000.

In human beings, the clinical course of the disease often evolves through 3 phases with characteristic manifestations.

(1) *Intestinal phase*: abrupt onset, fever, persistent headache, muscular pains, sweating, conjunctival injection, albuminuria; and gastro-intestinal signs, suggestive of typhoid, such as furred tongue, loose stools and meteorism. A pink maculo-papular rash distributed on the flanks and medial aspect of the thighs is not uncommon and lasts for 5–6 days.

(2) *Phase of remission* lasting 1–3 days.

(3) *Meningeal phase*, commonly starting on day 5 or 6 lasting 5–6 days: the pulse rate is rather slow in spite of a recurrence of fever; neck rigidity, positive Kernig and Brudzinski signs, photophobia, minor abnormalities of the cerebrospinal fluid (increased protein, lymphocytes 30–40 per cmm.). Paresis does not occur.

Jaundice does not occur, the outcome is always favourable, and complications are rare.

The diagnosis usually depends upon serological tests which are not always simple to interpret: coagglutinins (*i.e.* cross-agglutination) may confuse attempts to define the causative serotype and tests on a series of serum specimens may be necessary. However, with the causative serotype a negative zone may occur at the lower serum dilutions. Some knowledge of the patient's occupation may help the serologist to decide on the antigen suspensions which should be used in the agglutination tests.

The authors have used *L. pomona* antigens since 1945 and to date 143 of 3,467 (4·1%) of the routinely examined sera have been positive with it. Since 1950 about 13 positive sera have been detected annually. More positive sera are found during August to December. The regional distribution of human cases (serologically diagnosed) corresponds with that of *L. pomona* infection in pigs and horses—mainly in the east and west of the country.

The authors maintain that the economic, social and medico-legal importance of leptospirosis of porcine origin can no longer be denied; in certain cases all leptospiral infections can justifiably be regarded as occupational diseases.

Little mention is made of infection due to *L. mitis* (=*hyos*) except that the incidence is lower than that of *L. pomona* infections. *L. H. Turner*

CHUNG, Huei-Lan *et al.* **Leptospirosis: Epidemiological Studies in the Kwangtung Province, China.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 3, 347–62. [34 refs.]

Leptospirosis probably occurred in China in ancient times; and in the south and southwest regions it has long been known to the farmers as "yellow illness of the rice crop season". The first authentic report of [human] leptospirosis in China was by T'ANG TZE-KUANG [*Chinese Med. J.*, 1937, v. 51, 483]. The author and his colleagues have since isolated pathogenic leptospires from human patients in the following provinces: Kwangtung, Yunnan, Szechuan, Honan, Kiangsi, and Hunan; and others have succeeded in Chekiang, Fukien, Kweichow, and Kwangsi provinces. The present account deals with epidemiological studies in the central area of Kwangtung province where the incidence of leptospirosis has rapidly declined as a result of active public health measures.

Analysis of records of 310 patients (1951–1955) revealed that 86% were rice farmers, but all gave a history of wading; 85% were aged 15–49 years and males predominated (6·5:1), but most paddy field workers were adult males; the highest seasonal incidence (72·6% of all cases) was in the 4 months from July to October (peak, August) when rain, harvesting and long hours of work seemed to be contributory factors.

14 out of 16 isolated strains were identified as *Leptospira canicola* (5), *L. australis B* Zanoni (5), and *L. autumnalis* (4). Standard antisera used also included those for the following serotypes: *bataviae, australis* A (Ballico), *pomona, sejroe, grippotyphosa, bovis, hebdomadis,* and *icterohaemorrhagiae.*

Sera of 85 patients were examined by complement-fixation (CF) and agglutination-lysis (AL) tests: 83 (97·6%) were positive by CF. The cerebrospinal fluids of 30 patients were also tested and 21 (70%) were positive (CF). AL results accorded with those by CF testing except in some early specimens (low AL titres); but the AL tests were positive in all of 39 sera obtained after the 10th day of illness.

A serological survey (CF) of 670 farmers from 19 villages revealed that 299 (44·6%) were positive: the seropositivity rates among 6 subdivisions comprising this group ranged from 24·4% (41/168) to 73·2% (101/138). Peasants involved in 4 outbreaks of acute illness were investigated and the authors drew the following conclusions: (1) the illness was leptospirosis; (2) the incubation period was 5–12 days; (3) subclinical infection occurs; (4) persons with (CF) antibodies in their sera possess high immunity for a time; (5) frequent contact with infected water renders some persons relatively immune from leptospirosis. [The authors do not state whether or not some of these persons are included in the 607 previously mentioned].

Seropositivity (CF) rates in wild animals were as follows: *Rattus rattus flavipectus,* 94 out of 242 (38·8%); *Bandicota nemorivaga* 20/84 (23·8%); *Rattus bowersi,* 10/31; *Rattus rattus* and *Rattus rattoides,* 29/63 (46·0%); *Suncus murinus,* 4/8.

The rates for domestic animals were: dog, 53/55 (96·4%); buffalo and yellow cattle, 78/138 (56·5%); swine, 11/50; cat, 2/14. Ducks were positive (5/105, 4·8%), but not geese (4) or fowls (47): Fish (45) and frogs (4) were all negative.

Leptospires were isolated from the following animals: *Rattus r. flavipectus—L. autumnalis* (3); *L. canicola* (2), *L. australis* B (1), and *L. icterohaemorrhagiae* (1); *Bandicota nemorivaga—L. autumnalis* (4), *L. icterohaemorrhagiae* (2) and *L. canicola* (1); *R. bowersi—L. autumnalis* (1). Subsequently some of the authors isolated 3 strains of *L. pomona* from swine (2) and a dog. Mention is also made of the isolation of *L. pomona* from goats, of *L. autumnalis* from yellow cattle, and of unidentified strains from cats.

L. autumnalis was isolated, by immersing guineapigs, from water in paddy fields in 2 endemic localities.

The countryside of central Kwangtung consists of a low plain drained by tributaries meeting to form the Pearl River. In addition there is an extensive network of streams and irrigation channels with numerous ponds; the *p*H of waters sampled was 6·4–7·6, commonly 7·1–7·4. The land is widely cultivated; rice, sugar cane and vegetables are the main crops. Control measures [none novel] appear to have been effective but no details are given. *L. H. Turner*

WHEELER, W. E. & BORCHERS, Justine. **Vibrionic Enteritis in Infants.** *Amer. J. Dis. Children.* 1961, Jan., v. 101, No. 1, 60–66. [11 refs.]

This report concerns the first recognized examples of systemic infection in infancy by organisms of the group of spirella related to the well-known animal pathogens *Vibrio foetus* and *V. jejuni.* The 4 case-reports came from Colombus, Ohio, and describe 3 infants and a boy of 1½ years in whom the diagnosis was made retrospectively when the causal organism was isolated from his younger sibling.

In each patient the symptoms conformed to a single pattern in which recurrent diarrhoea, usually with low fever was associated with the passage of greenish stools containing mucous and flecks of blood. Marked dehydration occurred only in 1 patient.

Diagnosis was established by the isolation of the causal vibrio from the blood of the 3 infants, and presumptively by positive agglutination tests on the serum of the older child. The organism proved fastidious in its requirements and was cultured with difficulty in a broth medium containing agar (to give a varying 0_2 gradient) under 12% CO_2 at 42°C. in a candle jar. Even in this medium it tended to die out on subculture. Although the organism may be recognized in the stools as masses of motile cholera-like vibrios, attempts to culture them from the faeces were invariably unsuccessful. The organisms appeared to be sensitive to streptomycin and chloramphenicol but not to penicillin and neomycin.

This group of spirilla are of widespread distribution in the animal kingdom, for *V. foetus* is a common cause of abortion in cattle and sheep, while *V. jejuni* causes enteritis in cattle and can be transmitted to dogs: a closely-related type causes hepatitis in fowls. The disease

is thus a zoonosis, occasionally affecting the human race. In the first infant of this small series, infection was probably acquired from a puppy which suffered an attack of acute enteritis and with which the infant was in close contact. The source of infection in the other 3 children could not be traced.

The pathology of the disease, as deduced by analogy from cattle and from the autopsy findings in the only known human fatality, is a jejunitis with oedema and ulceration, the stomach, duodenum and colon escaping damage. *J. H. Walters*

VIRUS INFECTIONS

The order in this section is:—***General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.***

GORET, P. Sur la sensibilité éventuelle de l'homme aux infections virales canines apparentes ou latentes. Résultat d'une enquête sérologique conduite chez les étudiants de l'Ecole Vétérinaire d'Alfort. [**The Susceptibility of Man to apparent and latent Virus Infections of Dogs. Results of a Serological Investigation among Students of the Veterinary School, Alfort**] *Bull. Acad. Nat. Méd.* 1960, v. 144, No. 35, 846–52. [70 refs.]

Sera were taken from about 300 students in 1958 and 1959. These sera were tested in complement-fixation tests against dog distemper, canine hepatitis " contagious rhino-amygdalitis " and adenovirus, and in neutralization tests against 3 types of poliomyelitis virus. Positive results were found with all the viruses used; the numbers in each age-group are listed and the frequency of certain cross-reactions are given. The author concludes there is no relation between the content of antibody against distemper and poliovirus or between contagious rhino-amygdalitis and adenovirus; there may be a relation between adenovirus and canine hepatitis and between the latter virus and poliomyelitis. [The figures given do not seem to support the conclusions drawn; they are not fully tabulated and no statistical tests are reported.] *D. A. J. Tyrrell*

ORTEL, S. Serologische und epidemiologische Untersuchungen während einer Ornithose-Epidemie bei Angestellten eines Geflügel-Schlachthofes. [**Serological and Epidemiological Investigations during an Epidemic of Ornithosis among Employees of a Poultry Slaughterhouse**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 441–8, 3 figs. [21 refs.]

This paper describes the occurrence of ornithosis in the staff of a poultry slaughterhouse in Halle, Germany, during a period of 15 months from August, 1958, to October, 1959. Of a staff of 43, 35 were infected. Diagnosis was made on serological grounds by means of the complement-fixation test. Chemotherapy was employed and the majority of the infections ran a relatively mild course. Suggestions are made for the control of such outbreaks. These include the redesign of the slaughterhouse, the inspection of the incoming birds with the possibility of employing serological or intradermal tests in the recognition and exclusion of infected birds. Active immunization of the staff is discussed. *S. P. Bedson*

SIGG, R. H. Ornithose mit seltener, unfallbedingter infektion. [**An Unusual Accidental Ornithosis Infection**] *Schweiz. med. Woch.* 1961, Jan. 21, v. 91, No. 3, 85–7, 2 figs.

This paper describes an illness characterized by fever, bronchopneumonia and toxic myocarditis, which developed in a man a fortnight after having been bitten on the neck by an owl. A diagnosis of ornithosis was made on the clinical picture and a positive complement-fixation test. Despite high doses of terramycin (oxytetracycline) the illness ran a protracted course. [The diagnosis of ornithosis, though probably correct, could not be accepted as unequivocal. And it if were, it is unlikely that the infection resulted from the bird's bite, since it has been shown that living virulent psittacosis virus can be injected subcutaneously in man without producing disease. In this man's encounter with the owl there would, of course, be ample opportunity for inhaling virus coming from the bird.] *S. P. Bedson*

MATUMOTO, M., GOTO, T., NAKAMURA, H., MATSUSHIMA, S., NAITO, H., SHIODA, H. & OMORI, T. **Psittacosis in Japan: Analysis of Patients with Primary Atypical Pneumonia, Acute Bronchitis and other Diseases by means of Complement Fixation and Hemagglutination Inhibition Tests.** *Japanese J. Exper. Med.* 1960, Oct., v. 30, No. 5, 327–48, 1 fig. [43 refs.]

This paper records the results of a 3-year serological survey of psittacosis-group antibodies in human infections made at the Sagamihara National Hospital near Tokio. The complement-fixation and haemagglutination-inhibition tests were employed. The findings suggest that viruses of the psittacosis group have been playing a part in the causation of these cases and more particularly in primary atypical pneumonia, acute bronchitis and middle-lobe syndrome. *S. P. Bedson*

SCOTT, E. P. & STEIGMAN, A. J. **Accidental Isolated Primary Vaccinia of the Tongue.** *J. Pediatrics.* St. Louis. 1961, Jan., v. 58, No. 1, 77–9, 2 figs.

[This reads like a unique version of an American child delinquent story.] Child A, aged 5 years, was vaccinated on May 13th. On May 20th the lesion was " disturbed " by a neighbour's child. Soon afterwards Child B, aged 16 months, " a habitual biter ", bit sibling A on the vaccination site. Some days later B developed a sore on the tongue and fever and seemed quite ill. The mother, unaware of the rarity of such a lesion, diagnosed it as

"vaccination of the tongue" [almost certainly quite correctly] and painted it with gentian violet.

In the next act of the drama Child B took away the feeding bottle of Child C aged 4½ months sucked it and then, in a fit of rage, rammed it back into C's mouth. C. then proceeded to develop an ulcer of the tongue. This was associated with some general illness; a rise in haemagglutination inhibition titre subsequently took place and attempts to vaccinate with potent lymph proved unsuccessful.

The authors speculate on the rarity of accidental mucosal lesions in view of the activities of what they call normal children: and also on the likely difficulty which the children B and C may encounter in the future in establishing their lingual scars as evidence of successful vaccination. *J. Pickford Marsden*

SHEWARD, J. D. **Perianal Herpes Simplex.** *Lancet.* 1961, Feb. 11, 315–16, 1 fig. [12 refs.]

This is a description of the occurrence of herpes simplex on the perianal region of twins aged 2: the rash was limited to the napkin area. The father of the twins suffered from two "cold sores" on the lip at the same time and had used zinc and castor oil ointment which was also applied to the children's buttocks a few days later to treat napkin rashes. There is a short description of the clinical manifestations of herpes simplex and a photograph of the rash. *A. B. Christie*

MARTINEAU, B. Les virus dans les infections des voies respiratoires. [**Virus Infection of the Respiratory Tract**] *Canadian Med. Ass. J.* 1960, Dec. 31, v. 83, No. 27, 1427–30; 1961, Jan. 7, v. 84, No. 1, 43–9. [70 refs.]

The first of these papers is a summary of the main facts concerning the "new" respiratory viruses. The author reports the results of his attempts to demonstrate infection with adenoviruses in children in Montreal with "primary atypical pneumonia" and in babies and children up to 16 years with pharyngoconjunctivitis, pneumonia or meningo-encephalitis. He isolated from the throat and stools of a proportion of subjects in each group adenoviruses of types 2, 3 and 5 and of a serotype neutralized equally well by antiserum against types 3 and 7 and hence called 3–7. Complement-fixation tests only occasionally showed rises in antibody titre during the illnesses. The author suggests that this may be due either to the age of the patients and the type of infection they underwent, or to the fact that the antigen was not prepared from the serotype of virus with which they were infected, or that the patients were healthy carriers of the viruses isolated. The clinical and laboratory findings in the cases are summarized in 5 long tables and cannot be abstracted satisfactorily. Virus was recovered or an antibody rise was demonstrated in 85. [This study should have included serum neutralization tests and a parallel group of cases of non-respiratory disease. Then the question of the healthy carrier state might have been solved and the aetiological importance of the viruses much better defined.] *D. A. J. Tyrrell*

NEWMAN, J. O. **Transmission of Antibodies against Influenza Virus A across the Placenta.** *J. College General Practitioners.* 1960, Nov., v. 3, No. 29, 434–40. [12 refs.]

Maternal and cord blood were collected at the delivery of women who had had influenza or had been in contact with the disease during the epidemic of 1957–58. Antibody against influenza virus soluble complement-fixing antigen was found in many sera from all groups especially if influenza occurred shortly before delivery. Antibody tended to be present at delivery in foetal serum when influenza had occurred in early pregnancy although the antibody level in the maternal serum was low or undetectable.

[This is enterprising work from general practice, but a larger series with more thorough analysis and some statistical tests would be needed to prove the suggestions summarized in the last sentence of the abstract.] *D. A. J. Tyrrell*

CRAIGHEAD, J. E., SHELOKOV, Alexis, VOGEL, J. E. & PERALTA, Pauline H. **An Outbreak of Influenza B in Panama.** *Amer. J. Trop. Med. & Hyg.* 1961, Jan., v. 10, No. 1, 71–4, 1 fig.

"An outbreak of influenza occurring on the Isthmus of Panama in 1959 is described. Type B influenza viruses, antigenically similar to B/GL/54, were isolated and serological evidence of infection was demonstrated in a high proportion of persons tested. The outbreak began shortly after the opening of schools and the onset of the wet season and it is possible that these factors contributed to the spread of the virus. Tissue culture techniques were found to be practical for the study of influenza in this outbreak."

CHANOCK, R. M., WONG, Doris C., HUEBNER, R. J. & BELL, J. A. **Serologic Response of Individuals infected with Para Influenza Viruses.** *Amer. J. Pub. Health.* 1960, Dec., v. 50, No. 12, 1858–65. [11 refs.]

Children were studied in an orphanage nursery which had a mean weekly population of 52 children under 3 years of age. Outbreaks of infection with parainfluenza 1 (haemadsorption type 2) and 2 (haemadsorption type 2) viruses occurred. Para-influenza 1 virus was first detected in May 1958 and the epidemic lasted for the next 6 weeks. About 75% of the illnessess were of febrile upper respiratory type and lasted 1 to 7 days. 41 children had serological evidence of infection and virus isolations were made from 24 of these in monkey kidney tissue cultures by the haemadsorption technique; 4 isolations were made without serological confirmation. The complement-fixation (CF) technique was 4-fold less sensitive in detecting antibody rises than either the haemagglutination-inhibition (HI) or neutralization methods; 94% of children with acute laryngotracheobronchitis [ANDREWES *et al.*, this *Bulletin*, 1959 v. 34, 1056] developed CF antibody which suggested that the severity of illness might influence the level of antibody. The sensitivity of the

neutralization technique was increased by employing 10 instead of 100 TCD50 of virus so that low levels of antibody could be detected. 35 of 54 infants whose sera did not contain neutralizing antibody before the outbreak developed a 4-fold rise; only 7 (11%) already had antibody at a reciprocal titre of 32–128 and only 1 of these had a 4-fold or greater rise so that antibody appeared to protect.

The para-influenza 3 virus outbreak occurred in November–December 1957, spread rapidly (only 10 days between the first and last infections) and consisted of febrile upper respiratory illnesses and pneumonitis. 28 virus isolations were made and serological evidence of infection was shown in 42 children, the CF technique in this instance being as sensitive as the other two methods of detecting antibody rises. In contrast to the para-influenza 1 outbreak, 61% of the pre-epidemic sera contained neutralizing antibody and all the individuals who lacked antibody were infected during the outbreak. Although levels of neutralizing antibody of 64–512 seemed to confer some immunity, titres below this did not and this suggested that reinfection with para-influenza 3 virus was not uncommon.

Guineapig immune sera prepared against each of the viruses were tested in HI and CF tests. There were no cross-reactions, which implied that the viruses were distinct. However, about 30% of individuals infected with para-influenza 1 virus and 12% of those infected with para-influenza 3 virus developed HI antibodies against both viruses. The CF antibody response to para-influenza 1 virus was poor and heterotypic responses were common; the response to para-influenza 3 virus infection was seldom complicated by heterotypic para-influenza 1 antibody. These findings suggested the existence of a common antigen and that specific aetiological diagnosis was best made by virus isolation.

[It appears that the cases on which this paper is based have appeared in previous publications from this group of authors, see, for example, this *Bulletin*, 1958, v. 33, 621.] *D. Taylor-Robinson*

HOFMAN, B. & WILTERDINK, J. B. **Poliomyelitis Antibodies in Sera from the Netherlands, Curaçao, Surinam, St. Eustatius and Netherlands New Guinea.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 4, 397–406, 3 figs. [19 refs.]

A large-scale serological survey of the development of antibodies to the 3 types of poliomyelitis virus in the Netherlands and Curaçao has been made. Smaller samples from Surinam, St. Eustatius and Netherlands New Guinea were studied. It was found that antibodies to all 3 types of poliomyelitis virus were acquired more rapidly in Curaçao than in the Netherlands—Curaçao following the pattern reported for Cairo [PAUL *et al.*, this *Bulletin*, 1952, v. 27, 1092] and the Netherlands that seen elsewhere in temperate zones of the northern hemisphere. It was found that the proportion of people with high titres of antibodies fell with advancing years, as has been reported by LE BOUVIER [*ibid.*, 1958, v. 33, 412]. In the Netherlands the incidence of poliomyelitis and the absence of antibodies ran parallel with each other. The smaller areas seemed to follow the pattern of Curaçao except for St. Eustatius where type 2 infection was probably delayed a few years. *A. J. Beale*

BERKE, Z. & ARI, A. Türkiyenin Akdeniz ve Dogu Kardeniz bölgesinde O-9 yaslari arasinda olan çocuklarda Poliyomiyelitis antikor seviyesi. [**Poliomyelitis Neutralizing Antibody in Sera from Turkish Children**] *Türk Ijiyen ve Tecrübî Biyoloji Dergisi.* Ankara. 1960, v. 20, No. 3, 342–7. English summary.

Sera were collected—500 in all—from the Mediterranean Coast and the Black Sea Coast and sent to the United States. Antibodies to poliomyelitis virus (all 3 types) were present in about 40% of children aged 1–2 years, and in 80–100% of children aged 3–9.

SALVAGGIO, L., ALBANO, A. & MORMONE, V. Osservazione e considerazioni su di un episodio epidemico di poliomielite in una collettività infantile vaccinata. [**Observations and Considerations on an Epidemic of Poliomyelitis in a Children's Home**] *Ann. Sclavo.* Siena. 1960, Nov.–Dec., v. 2, No. 6, 595–609, 2 figs. [28 refs.] English summary.

In the Campania region during 1958 there were 2,368 cases of poliomyelitis [this *Bulletin*, 1960, v. 35, 676], equivalent to an incidence rate of 50 per 100,000. This paper deals with an outbreak which occurred in a children's home in Naples, soon after a routine immunization procedure had been set in motion, with vaccine of Salk type and also a polyvalent vaccine against tetanus, whooping cough and diphtheria. Salk vaccine was given at 2½–3 months and repeated at 3½–4 and 8–10 months of age; the polyvalent vaccine was given at 3–3½ months, followed by 2 further doses at intervals of 25–30 days.

There were 430 children in the home, 278 being infants under 1 year and 152 being aged 1–3 years, when the first case occurred on 11 October, 1958; the last paralytic case set in on 19 November, 1958. There were 10 paralytic cases, 4 in infants from 2 wards on the 3rd floor and 6 in older children from 2 wards on the 2nd floor. The paralysis affected a lower limb and there were no bulbar paralysis and no fatalities: 7 of these children had had a subcutaneous injection of the polyvalent vaccine in the buttock 4 weeks before the paralysis appeared and the authors do not consider that there was any causal connexion. There were 47 other children who suffered a febrile non-paralytic illness at the time, with gastro-intestinal and nervous manifestations.

When the first case occurred 230 children had not yet received any immunization injections. All the children in the affected wards were given at once 2 cc. of gamma globulin (from a mixed adult bank) intramuscularly and the routine of active immunization was not suspended.

With an interval of 1 month, 2 specimens of faeces and 2 of blood were taken from each of 32 children, of whom 8 had developed paralysis, 5 had had a non-paralytic illness and 19 were contacts with no clinical signs or symptoms. Type 1 virus was isolated from the 8 paralytic

and 2 of the non-paralytic patients and from 9 contacts. A rise in antibody titre for Type 1 virus was found in 4 of the paralytic patients and in 15 other subjects.

Four children developed the paralytic illness 1–3 days after having received gamma globulin.

J. Cauchi

MOLNER, J. G. & AGATE, G. H. **Final Report of Poliomyelitis Epidemic in Detroit and Wayne County, 1958.** *Pub. Health Rep.* Wash. 1960, Nov., v. 75, No. 11, 1031–43, 3 figs.

This epidemic [this *Bulletin*, 1959, v. 34, 735] was of a scale reminiscent of pre-vaccine days with 412 paralytic and 462 non-paralytic cases in a population of approximately 3 million persons. There were 25 deaths and 224 cases with significant or severe residual paralysis. 60% of the paralytic attacks were in children under 5 years of age. The heaviest incidence fell on the non-whites with an estimated attack rate of 57 per 100,000 compared with 5·2 per 100,000 in the white population. The incidence was particularly heavy in the centre of the city, an area of low economic status, high population density and a low vaccination rate. Less than 50% of the children in its elementary schools had had 3 inoculations and about 35% had had none. An extensive immunization programme was undertaken and a full course of 3 injections was offered to all, regardless of the patient's ability to pay. Some 2 million injections were given. The epidemic commenced late in July, reached its peak in September and ended in November. Type 1 predominated.

Such an outbreak can best be prevented by continual searching for areas of low artificial protection, making vaccination readily available to all and resorting to intensive personal persuasion or education to encourage inoculation. The peak occurrence of paralytic cases in the second year of life indicates not only the urgent need to give protection as early as possible but suggests that an intensive follow-up of infants in their first year of life to ensure vaccination would be the means of building up the community's protection.

A. Bradford Hill

MÜLLER, F. & MEER, Ursula. Untersuchungen über den diagnostischen Wert der Komplementbindungsreaktion mit Poliovirus-Antigenen. **[Investigations of the Diagnostic Value of the Complement-Fixation Test with Poliomyelitis Virus Antigens]** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 1, 50–78, 4 figs. [30 refs.]

An investigation has been made of the diagnostic value of the complement-fixation tests with antigens consisting of heat-inactivated poliomyelitis virus of the 3 types grown in monkey kidney cells and also of infective virus grown in HeLa cells and purified with difluortetrachloroethane [this *Bulletin*, 1960, v. 35, 1058]. With the former antigen a 4-fold or greater rise in titre to at least one type of virus was seen in only 79 (33%) of 243 patients with paralytic poliomyelitis, 13 (24%) of 54 with aseptic meningitis, and 8 (40%) of 20 patients suffering from isolated facial palsy. The proportions were no higher in 60 patients from all 3 groups from whom type 1 poliomyelitis virus had been isolated. Positive results were obtained somewhat more frequently in the older age-groups. The titres of antibodies to the 3 types of virus in 74 patients who were investigated several times for up to 93 days after the onset of illness are presented in a table. The individual highest titres were usually observed before the 30th day of illness. The type specificity of the test was not very high. In a study of the effect of variations in the technique of the test the greatest proportion of positive results was obtained by the serum-dilution method, with the purified infective antigen.

D. J. Bauer

EVANS, C. A. **Factors influencing the Occurrence of Illness during Naturally Acquired Poliomyelitis Virus Infections.** *Bact. Reviews.* 1960, Dec., v. 24, No. 4, 341–52, 2 figs. [Numerous refs.]

Naturally occurring polioviruses may have high or low virulence for man but pertinent studies of viruses have not revealed any viral characteristics to account for the differences. Even the most virulent strains cause paralysis in a very small proportion of patients affected. It would appear that the characteristics of the infecting virus are less important than some other factors in determining the occurrence of paralytic disease. As regards the infected person it is well known that pregnancy, tonsillectomy and injections influence the development of paralysis but these factors operate in only a small proportion of cases. It is possible that the method of infection or size of infecting dose may be important and the author refers to an outbreak concentrated in one part of a military families' settlement where faecal pollution of water supply appeared to be the responsible factor: evidence that infection was widespread throughout the settlement was shown serologically but paralytic attacks were restricted to the area of faecal pollution. Simultaneous infection with a second virus, *e.g.*, Coxsackie, may occur owing to faecal pollution of water supplies and may act synergistically with poliovirus to increase the likelihood of paralysis. Studies on the protection of cells by interferon may yield important information as such cells are obviously analogous to the person who remains well though infected with poliovirus.

A. B. Christie

KENDALL, E. J. C., MILLER, Ann & TOBIN, J. O'H. **Further Observations on the Persistence of Antibody in Adolescents after a Third Dose of Killed Poliomyelitis Vaccine.** *Brit. Med. J.* 1961, Jan. 21, 176–7, 3 figs.

In a previous study the authors [KENDALL *et al.*, this *Bulletin*, 1960, v. 35, 1017] found that 18–24 months after the end of a poliovaccination course consisting of 2 primary doses and a booster 6–12 months later, the antibody levels had fallen to about one-fifth. Specimens for antibody titration were taken from 30 of these public-schoolboys 27–33 months after the complete course of vaccine. None had any antibodies to poliomyelitis virus before vaccination and all had antibodies to all 3 types 18–24 months later and all but 1 (lacking antibodies to Type 1 only) still had them at 27–33 months. The rate of

decline had slowed, being 22% for Type 1, 23% for Type 2 and 15% for Type 3. The rate of decline has fallen from about 50% per year to less than 30% per year. The results were most variable for Type 1, especially in those people who had no residual antibodies when given the 3rd or booster dose. The authors conclude that, given a more potent Type 1 component, killed poliovaccine can be considered satisfactory, requiring no more booster doses than are currently given for other prophylactics.

A. J. Beale

SNOW, D. J. R. & LEWIS, B. H. **Salk Vaccination: Reactions and Sequelae. Observations in Western Australia.** *Med. J. Australia.* 1960, Dec. 3, v. 2, No. 23, 890–92.

During the administration of 1·3 million doses of Salk vaccine to about 480,000 people, a very low incidence of untoward reactions was observed. These are described. A few children developed transient rashes usually similar to rubella. 2 people suffered from urticaria and 2 from allergic dermatitis. 1 case of streptomycin sensitivity and 2 of penicillin sensitivity were seen. 4 adults suffered from pains in the upper arm or shoulder persisting for several weeks. In addition, 3 adults suffered from muscular weakness with subsequent wasting. There was one case of asthma and one anaphylactoid reaction. These cases were similar to those that have been described following other prophylactic inoculations. *A. J. Beale*

MERRILL, R. E., BATSON, R. & KINSMAN, Deborah. **Vaccination Status of Patients in an Outbreak of Acute Poliomyelitis.** *Amer. J. Dis. Children.* 1960, Dec., v. 100, No. 6, 857–60, 2 figs.

During the summer of 1959 there were 69 cases of confirmed poliomyelitis in the middle Tennessee area. 43 of 65 studied had not been vaccinated with killed poliovaccine, 15 had had 1 or 2 doses, 4 had had 3 doses, the last within 1 year of onset. The majority of the patients were children under school age. Although the number of cases in fully vaccinated individuals was low, these patients nonetheless sometimes suffered severe paralysis. Indeed, the authors could find no evidence that vaccination mitigated poliomyelitis infection. *A. J. Beale*

PAYNE, A. M. M. **Oral Immunization against Poliomyelitis.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 6, 695–703.

This is an authoritative review of some of the problems associated with oral immunization against poliomyelitis. The advantages of oral vaccine are ease and economy of administration together with ready acceptance of the vaccine. Earlier hopes that 1 dose would suffice seem ill-founded in fact. The vaccine, being living, requires careful handling to ensure continued potency, which may be particularly difficult under tropical conditions. There is no simple test of take rate, which has to depend on virological tests for excreted virus or antibody development. There are 2 main questions: is the vaccine safe for the individual and for the community; is it effective under the conditions used? After reviewing briefly the large-scale trials that have been performed with the Sabin, Koprowski and Lederle strains, the author concluded that the vaccines are safe both for individuals and for communities where poliomyelitis is a disease of infancy. He believes (though noting contrary opinions) that Sabin's strains at least have proved safe even in communities with substantial numbers of non-immune adults. Too little time has elapsed to determine the efficacy of the vaccine but, in view of the high serological conversion rates, it will almost certainly prove effective though repeated doses are probably necessary.

Some of the recommendations of the WHO Expert Committee Report [this *Bulletin*, 1961, v. 36, 276] are briefly reviewed. Sabin's type 1 and 2 strains are considered the most suitable. All the type 3 strains are too genetically unstable for a preference to be expressed. Koprowski's type 1 spreads poorly to contacts and capacity to spread is considered especially desirable by some authorities, though other authorities consider this capacity a potential source of danger. Methods to overcome interference by other enteroviruses and to mark the genetic characters of strains are required. Nonetheless, the author looks forward to the steady extension of the use of attenuated poliovaccine and perhaps the eventual eradication of poliomyelitis.

A. J. Beale

SMORODINTSEV, A. A., DROBYSHEVSKAYA, A. I., BULYCHEV, N. P., CHALKINA, O. M., GROISMAN, G. M., ILYENKO, V. I., KANTOROVICH, R. A., KURNOSOVA, L. M., VASILYEV, K. G., VOTYAKOV, V. I. & ZHILOVA, G. P. **Immunological and Epidemiological Effectiveness of Live Poliomyelitis Vaccine in the USSR.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 6, 705–25, 3 figs. [12 refs.]

This is a long paper about Russian work on attenuated poliovaccine. Attenuated vaccine is considered to be the only practical measure of preventing poliomyelitis. The importance of the long-lasting intestinal immunity induced by living vaccine in breaking the chain of infection is stressed. Type 1 vaccine followed by mixed types 2 and 3, and sometimes again by mixed types 1, 2 and 3, produces antibodies in over 95% of the population, filling the gaps in naturally acquired antibody. Areas where the vaccine was widely used failed to experience the seasonal rise in poliomyelitis incidence still noted in unvaccinated areas. Poliomyelitis was rare in vaccinated individuals but did occur in contacts, suggesting that spread of the vaccine virus to contacts cannot be relied on to protect contacts. However, in some areas the incidence of poliomyelitis was higher in internal controls (*i.e.* contacts) than in external controls (*i.e.* unvaccinated people in the same general area). In all areas the incidence among the vaccinated was substantially less than in control groups, usually by a factor of about 10-fold.

[This is a long and detailed paper which should be read in full. It is not always easy to find the documentation for statements made.] *A. J. Beale*

D'Alessandro, G., Dardanoni, L., Brancato, P. & Gullo, A. Somministrazione di virus polio 1 attenuato LSc di Sabin a bambini viventi in comunità con alta frequenza di infezioni enterovirali. **[The Administration of the Sabin LSc Strain of Attenuated Type 1 Poliomyelitis Virus to Children Living in a Community with a High Incidence of Enterovirus Infection]** *Riv. Istituto Sieroterap.* Ital. 1960, July–Aug., v. 35, No. 4, 425–39. [10 refs.] English summary.

Cytopathogenic agents could be isolated from 270 (69%) of 390 rectal and pharyngeal swabs taken from 62 children aged up to 3 years living in an institution, 5 of whom had been given type 1 live attenuated poliomyelitis vaccine containing the LSc strain. The agents isolated included poliomyelitis type 3, ECHO types 1, 7, 9, 10 and 12 and Coxsackie B5 viruses. In serial investigations carried on up to 59 days after vaccination it was not possible to recover type 1 poliomyelitis virus from the vaccinated children or from their contacts, or to detect type 1 neutralizing antibody. The failure of the vaccine virus to take was attributed to interference from the enteroviruses which were already present

D. J. Bauer

Ruegsegger, J. M. & Delery, M. **Trivalent Poliomyelitis Vaccine administered orally in a Cloistered Community.** *New England J. of Med.* 1960, Sept. 22, v. 263, No. 12, 596–8.

123 monks at St. Joseph's Abbey, Worcester, Massachusetts were given an oral poliovaccine containing $10^{6.1}$ TCD50 of each type of virus. Before vaccination approximately 50% lacked antibodies to one or other type of poliomyelitis virus. 38 lacked antibodies to types 1 and 3, and 39 to type 2. 30 days after vaccination 82% had antibodies to all 3 types. None now lacked antibodies to type 1, 11 to type 2, and 2 to type 3. 23 of the monks had had Salk vaccine (1–4 doses not individually specified) and 4 lacked type 3 antibodies and 1 lacked them to both type 1 and type 3. During this small trial no symptoms attributed to the vaccine were suffered by any member of the Abbey community whether vaccinated or not.

A. J. Beale

Lerner, A. M., Klein, J. O., Levin, H. S. & Finland, M., with technical assistance of Priscilla Bills & Ann Ewalt. **Infections due to Coxsackie Virus Group A, Type 9, in Boston, 1959, with special reference to Exanthems and Pneumonia.** *New England J. of Med.* 1960, Dec. 22, v. 263, No. 25, 1265–72, 1 fig. [52 refs.]

This is a record of 16 cases of infection with Coxsackie virus Group A type 9 seen at Boston City Hospital from July to October 1959. The virus was isolated from throat, rectum, blood and cerebrospinal fluid: in the 1 fatal case it was isolated from lung and liver. Abacterial meningitis, pneumonia and rashes were the main symptoms: the rashes were vesicular in 6 patients, petechial in 3 and maculopapular in 2. 4 patients had acute respiratory symptoms, 4 had abacterial meningitis and 7 had rashes only.

A. B. Christie

Lerner, A. M., Klein, J. O. & Finland, M., with the technical assistance of Priscilla Bills. **A Laboratory Outbreak of Infections with Coxsackie Virus Group A, Type 9.** *New England J. of Med.* 1960, Dec. 22, v. 263, No. 25, 1302–4, 1 fig. [13 refs.]

A small outbreak of Coxsackie A9 infection, initially acquired in a virus laboratory, is described. On April 6th, 1960, P.B. was processing stools containing Coxsackie A9 and 2 days later became ill and had serological evidence of infection. A household contact, J.F., had no evidence of infection. J.K., who also worked in the laboratory, was infected, becoming ill on April 9th, 1960. His 2 children became ill with Coxsackie A9 infection but his wife, L.K., escaped infection. Another laboratory worker, A.M.L., conveyed infection to his wife, son and son's nursemaid. This last patient did not transfer infection to her husband. Thus, in all, there were 7 cases among 11 contacts. A.M.L. had a low titre of antibodies in his acute phase serum but showed no rise, though he clearly carried the virus home. 8 out of 10 workers in adjacent laboratories had no antibodies to Coxsackie A9 when tested 3 months later. The clinical manifestations varied slightly but consisted of some combination of the following: malaise, fever, pharyngitis, rubelliform rash, rhinorrhea and meningitis.

A. J. Beale

Moossy, J. & Geer, J. C. **Encephalomyelitis. Myocarditis and Adrenal Cortical Necrosis in Coxsackie B3 Virus Infection. Distribution of the Central Nervous System Lesions.** *Arch. Pathology.* 1960, Nov., v. 70, No. 5, 614–22, 7 figs. [16 refs.]

The authors describe the histological details of the central nervous system in a fatal case of Coxsackie B3 virus infection occurring in a baby 3 days old in New Orleans. Parenchymal lesions were composed mainly of mononuclear phagocytes and proliferating rod cell forms of microglia: they occurred more frequently in grey than in white matter and were present in the brain stem, cerebellum and cervical spinal cord but, except for one small lesion, absent from the cortex. Differential diagnosis from other possible causes of encephalitis is discussed. Brain stem lesions combined with myocarditis and adrenal necrosis should suggest Coxsackie virus infection. Herpes simplex may produce a similar picture: the demonstration of Type A intranuclear inclusions would help. Differentiation from poliomyelitis is difficult and the lesions produced in the spinal cord of newborn mice may be identical [this *Bulletin*, 1959, v. 39, 319]: the distribution of lesions in the human brain and cord may help, the reticular substance in the medial and tegmental core of the brain stem and the cerebellar roof nuclei being regularly damaged in poliomyelitis but not in the case here described. Cytomegalic inclusion disease involves the periventricular areas; toxoplasmosis produces a widespread granulomatous encephalitis; the arthropod-borne encephalitides tend to involve mainly the cortical and subcortical areas and are not usually associated with myocardial, hepatic or adrenal lesions

A. B. Christie

NASEMANN, T., STETTWIESER, E. & RÖCKL, H. Zur Klinik des variablen infektiösen Exanthems. Beobachtungen anlässlich der Epidemie im Herbst 1958. **[The Clinical Features of Exanthema Infectiosum Variabile; Observations during the Autumn Epidemic of 1958]** *Münch. Med. Woch.* 1959, Mar. 20, v. 101, No. 12, 485–9, 508, 5 figs. (2 on pl.) [25 refs.]

The English summary appended to the paper is as follows :—

" The authors report on 100 closely investigated cases of exanthema infectiosum variabile which occurred epidemically in Munich.

" The clinical picture and the course of the disease are described in detail.

" The problem of viral aetiology of the infectious exanthema and its possible similarity to the so-called fifth malady is discussed. Hitherto obtained results of isolation tests are referred to."

ENDERS-RUCKLE, G., HEITE, H. J. & SIEGERT, R. Klinische und virologische Studie über das akute epidemische Exanthem (sog. " Bläschenkrankheit "). I. Mitteilung. Besprechung der Krankheitsfälle und der zugehörigen Isolierungsversuche. **[Clinical and Virological Studies on the Acute Epidemic Exanthem known as Blister Disease. I. Review of Cases and Experiments on Isolation of an Infection Agent]** *Münch. Med. Woch.* 1959, Mar. 20, v. 101, No. 12, 490–94, 506–8, 7 figs. [23 refs.]

The English summary appended to the paper is as follows:—

"After a brief survey of the spread of epidemic exanthema which occurred during the second half of 1958 in the German Federal Republic, the authors refer to the sundry nosological classification of the disease which no doubt showed various similarities to the 'Erythema infectosum' (fifth malady). However, important epidemiological, nosological and symptomatological differences were noted which are admitted even by those authors who considered this epidemic as being identical with the fifth malady. Other authors, however, hold that this classification is not justified. This problem can be clarified only from the aetiological view-point. Therefore, isolation tests of an aetiological agent in 14 characteristic and carefully described cases of the 'blister-disease' were made. 12 cytopathogenetic agents could be isolated from throat gargle water and stool specimens cultivated on cultures of kidney-tissue of monkeys of various origin and on cultures of human tissue. 6 of these strains which were carefully examined as to their cyto-pathogenetic behaviour and as to tissue affinity in cell-cultures showed far-reaching conformity. Identification tests, which are reported upon the following, however, indicated that the agents showed no complete serological conformity, but are of two different types with relations to the Echo-group as well as to the Coxsackie group."

(L.292)

KIMMIG, J., RHODE, B. & HAGENOW, J. Zur Ätiologie eines epidemisch aufgetretenen, infektiösen Exanthems sogenannte Kieler-, Osnabrücker- oder Bläschen-Krankheit. (Isolierung eines vermehrungsfähigen Agens mit cytopathogenem Effekt in der Gewebekultur.) **[The Aetiology of an Epidemic Infectious Exanthematic Disease, known as the Kiel, Osnabrück or Blister Disease. (Isolation of a Self-Reproducing Agent Cytopathic in Tissue Culture)]** *Klin. Woch.* 1959, Jan. 1, v. 37, No. 1, 12–13, 4 figs.

A translation of the authors' summary is as follows:—

" 1. A self-reproducing agent has been demonstrated in the faeces of a patient with this disease.

" 2. Tissue cultures of fowl fibroblasts and monkey kidney cells can be infected.

" 3. The cell layer reacts to inoculation with the virus, showing a cytopathic effect." *Charles Wilcocks*

SCHÖN, H. & WÜST, H. Untersuchungen über eine Hepatitisepidemie. **[An Epidemic of Hepatitis]** *Deut. med. Woch.* 1961, Feb. 17, v. 86, No. 7, 281–7, 9 figs. [12 refs.]

In a previous short paper [this *Bulletin*, 1960, v. 35, 475], the authors reported on an epidemic of hepatitis which had occurred in Poppenlauer, a rural district in Lower Franconia (an area in the Main river valley).

The paper now presented contains the observations on the clinical, epidemiological and therapeutic features of the epidemic together with the results of laboratory investigations.

Since 1938 there had been only 1 or 2 cases of hepatitis annually (except for 1956 when there were 5 cases) in Poppenlauer and these cases were only in adults. In the winter months of 1958–59 however, when the epidemic began, cases occurred in children and young persons. The epidemic reached its peak in June 1959 and then gradually receded. In all a total of 185 cases of hepatitis occurred in the population of 1,800 persons. 157 of these cases were in children up to 14 years of age of whom there were 460 in the population. The highest incidence was in the 4–6 and the 12–13-year age-groups.

The symptoms were loss of appetite, tiredness, nausea and vomiting but icterus of the skin was seen in only 31%. Bilirubinuria was manifest in over half of the children.

Much of the paper is devoted to the results of serum enzyme activity studies—glutamic-pyruvic and glutamic-oxalacetic transaminases and lactic and sorbitol dehydrogenases. The glutamic-pyruvic transaminase was found to be the most sensitive for diagnostic and epidemiological purposes. Of the serum lability tests only the thymol turbidity test was found to be of value but was of little help in assessing progress.

Epidemiological investigations made in the area showed that poor hygienic conditions favoured spread of the infection and that incidence was high in large families. It was estimated that asymptomatic infection occurred in at least 20% of the population. *M. E. Delafield*

CLARK, W. H., BECK, M. D., EDWARDS, Geraldine B. & DRAKE, R. M. **A Special Study of Infectious Hepatitis in the General Population of Three Counties in California.** *Amer. J. Trop. Med. & Hyg.* 1960, Nov., v. 9, No. 6, 639–51. [16 refs.]

During the years 1954 and 1955 the prevalence of infectious hepatitis in the United States was particularly high, and it was possible to study the disease on an adequate scale in its endemic setting in the population. For this purpose 1,546 patients in 3 counties in California were visited in their homes, twice at a 40-day interval, during a period of 2 years. The attack rates were most frequent in the age-groups 5–9 and 30–39, but only slightly more frequent than in the age-groups 10–14, 20–24, and 25–29. The secondary attack rate in 1,160 households was 3·5% for all ages—a relatively low figure probably because 40% of the household population studied received prophylactic gamma globulin; in the protected group the figure was 2%, which was in marked contrast with that in the unprotected group (18%). Sequelae were found in 24·9% of the patients, including liver damage in 12·6%. The fatality rate was 3·7% for all ages, but at ages over 40 it was over 15% although the incidence at these ages was low. The prognosis over 40 years of age is therefore relatively poor, as it is also in poliomyelitis. *H. Stanley Banks*

MAXWELL, N. G. **Incidence of Serum Hepatitis in Recipients of Thymol Turbidity-Screened Blood or Aged Liquid Plasma.** *Amer. J. Clin. Path.* 1960, Dec., v. 34, No. 6, 518–25, 1 fig. [17 refs.]

Groups of recipients of blood and of plasma were followed up to determine the incidence of serum hepatitis, and the results were correlated respectively with the thymol turbidity values recorded for the donors' blood or with the age of the plasma at the time of transfusion. The incidence of hepatitis in recipients of blood with abnormal and normal values for thymol turbidity was virtually identical—0·685% and 0·692% respectively. Determinations of thymol turbidity (and also of thymol flocculation and total bilirubin) seemed to be of no value in detecting carriers of hepatitis viruses. Similarly, storage of liquid plasma at room temperature for 6 months did not seem to be sufficient to eliminate the occurrence of hepatitis.

Donors of blood, or packed red cells, to a patient who contracts hepatitis between 14 and 180 days after transfusion should be regarded as possible virus carriers, until better tests are developed. *H. Stanley Banks*

TAGIL'TSEV, A. A. **Certain Comparative Ecological Data on Gamasid Ticks occurring in the Nests of Birds and Small Mammals in an Enzootic Focus of Tick-Borne Encephalitis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 5, 860–69, 1 fig. [25 refs.] [Translated from Russian.]

Studies were made of gamasid mites associated with birds and small mammals in the Kemerovo Oblast'. 27 species were collected from small forest mammals and their nests comprising permanent ectoparasite species, obligate haematophagous species and symbiont species some of which are predators on the other species. The infestation of birds and their nests depended on their nesting habits: heavy infestations were associated with birds nesting in hollow trees. Russian spring-summer encephalitis virus was isolated from *Dermanyssus hirundinis* collected from the nests of 2 starlings. This species is capable of withstanding large changes in temperature and humidity and can starve for up to 11 months at low temperatures. They can therefore persist successfully in deserted nests. The temperature and humidity of the nests and burrows of small mammals is much more constant but when deserted the facultative haematophagous and predatory species become predominant and the obligate haematophagous species tend to disappear. It is suggested that gamasids in nests may maintain Russian spring-summer virus between seasonal outbreaks in man and that the infection of *Ixodes* ticks occurs when they feed on birds and mammals viraemic after infection by gamasids. [Experimental evidence is required to show that gamasids can transmit the infection.] *C. E. Gordon Smith*

ALIFANOV, V. I., ZAKORKINA, T. N., NETSKY, G. I. & FEDOROV, V. G. **[Experimental Data relative to the Role played by Gamasoidea in Transmission of the Tick-Borne Encephalitis and Omsk Hemorrhagic Fever Viruses]** *Med. Parasit. & Parasitic Dis.* Moscow. 1961, v. 30, No. 1, 24–6, 121–2. [In Russian.]

The English summary appended to the paper is as follows:—

"In areas endemic of Omsk hemorrhagic fever, of recent years, there has been noted an intensive epizootic among populations of Ondatra zibethica (introduced into the region), that tends to occur every time during a rise of their numbers. This epizootic is produced by the virus of Omsk hemorrhagic fever (A. V. Gagarina. O. V. Ravdonikas, V. E. Zimina and others).

"The most likely transmission agent serving as a link between the natural focus and ondatra appears to be: Arvicola terrestris, which partakes in the circulation of the virus, this being corroborated by the presence in 6·2% of these animals of complement fixing antibodies to the virus of the Omsk hemorrhagic fever, which according to its antigenic properties stands very close to that of tick-borne encephalitis.

"An exchange of Gamasoidea between Arvicola and Ondatra has been established, this occurring through their mutual contacts on the lakes.

"The virus of Omsk hemorrhagic fever has been isolated from the gamasids Laelaps muris, Hyperlaelaps amphibius, Hirtionissus isabellinus, Haemolaelaps glasgowi, combed from experimentally infected Arvicola with firmly established viremia in their blood. The virus has also been isolated from some of the Laelaps multispinosus combed from experimentally infected Ondatra, caught in a healthy state under natural conditions. Following transplantation of the other part of the Laelaps multispinosuns to the healthy Ondatras the latter contracted Omsk hemorrhagic fever, this being ascertained by the isolation of the virus from them."

ARAKAWA, S., NAGASHIMA, H. & KANEKO, T. **Experimental Study on Measles Virus. 7th Report: Vaccination against Measles by the Mouse-Fixed Measles Virus.** *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 481–97. [20 refs.]

The authors report the results obtained under practical conditions in 1955 and 1957 in trials of a concentrated measles vaccine prepared from the supernatant fluid of homogenates of chick embryos and chorioallantoic membranes infected with the OHKI [this *Bulletin*, 1954, v. 29, 1134] and WATANABE strains of mouse-adapted measles virus. The work described has been previously published in Japanese. Complete protection over a period of 8 months during subsequent epidemics of measles was observed in 190 of 210 (90·47%) susceptible children given 3 doses intradermally at intervals of 1 week of 0·4 cc. of vaccine inactivated with 0·01% sodium ethylmercurithiosalicylate.

Protection of similar extent was also obtained in a number of other groups ranging in size up to 108 persons, and the results are summarized in a table. [See also this *Bulletin*, 1960, v. 30, 942.] *D. J. Bauer*

OKUNO, Y.; SUGAI, T.; FUJITA, T.; YAMAMURA, T.; TOYOSHIMA, K.; TAKAHASHI, M.; NAKAMURA, K.; KUNITA, N. **Studies on the Prophylaxis of Measles with Attenuated Living Virus. II. Cultivation of Measles Virus isolated by Tissue Culture in Developing Chick Egg** [OKUNO, SUGAI, FUJITA, YAMAMURA, TOYOSHIMA, TAKAHASHI, NAKAMURA & KUNITA]. *Biken's J.* Osaka. 1960, Mar., v. 3, No. 1, 107–13. **III. Inoculation Tests in Man and Monkey with Chick Embryo Passage Measles Virus** [OKUNO, TAKAHASHI, TOYOSHIMA, YAMAMURA, SUGAI, NAKAMURA & KUNITA]. *Ibid.*, 115–22.

(1). The Edmonston and Toyoshima strains of measles virus adapted to FL cells could be maintained in fertile eggs by serial passage. Eggs on the 7th day of development were inoculated in the allantoic or amniotic cavities and incubated for 7 days; the respective membranes and fluids were then removed and homogenized together and used as passage material. The presence of virus was demonstrated by inoculation of FL cells, and by an interference method based on the ability of measles virus multiplying in the chorio-allantois to interfere with the multiplication of mumps virus inoculated 4 days later.

(2). 19 children presumed to be susceptible to measles were inoculated intranasally with 0·5 cc. of the Edmonston strain after 1 passage in the allantoic cavity; after 7 days 5 developed a febrile illness with a very scanty exanthem resembling a mild attack of measles. An 8–64-fold rise in titre of complement-fixing antibody developed in these children and also in 2 of the 14 who had shown no signs of illness. A rise in antibody titre in the absence of symptoms was also seen in 9 cynomolgus monkeys which received material from the 2nd and 16th chorio-allantoic passages of the Toyoshima strain of measles virus.

D. J. Bauer

MINISTRY OF HEALTH. **Reports on Public Health and Medical Subjects No. 101. Rubella and other Virus Infections during Pregnancy** [MANSON, Margaret M., LOGAN, W. P. D. & LOY, Ruth M.]. **Based on data assembled during 1950–1957 by The Medical Officers of Health of the Local Health Authorities of Great Britain.** pp. v + 101, 4 figs. (1 coloured folding). [33 refs.] 1960. London: H.M. Stationery Office. [7s.]

Since the early 1940's various reports have been concerned with the possible association between virus infection during pregnancy and congenital malformations of the foetus. In particular the effect of rubella in pregnancy has been the subject of much work and HILL and his colleagues [this *Bulletin*, 1958, v. 33, 551] have shown by pooling their own and other comparable data that 6 (50%) infants with major congenital defects resulted from 12 pregnancies to women who had rubella in the first 4 weeks of pregnancy compared with 5 (25%) out of 20 in the second 4 weeks, 3 (17%) out of 18 in the third and 3 (6%) out of 54 whose rubella was contracted after the third trimester. In order to assess such risks with precision, the Society of Medical Officers of Health, at the request of Sir Wilson JAMESON, then C.M.O. of the Ministry of Health, sponsored a prospective study of large numbers of pregnancies and all medical officers of health in England and Wales and Scotland agreed to participate. The Ministry and the General Register Office planned the investigation, administered it and analysed the results which are now published.

In brief the plan was to detect, as early in pregnancy as possible, women who contracted certain virus infections (rubella, measles, mumps, chickenpox and poliomyelitis) and to compare the results of their pregnancies with those of a control group who had no virus infection during pregnancy. The control group was limited to such women born on the 31st of any month. Doctors and midwives questioned patients at all ante-natal visits about illnesses they had experienced and the two groups of patients were accumulated during the period July 1950 — December 1952. "Virus" and "control" patients were kept under observation until the end of pregnancy and live born children were observed for 2 years; they had medical examinations shortly after birth, at age 1 and at age 2 years. The numbers of cases available for analysis, with the number registered in brackets, were 5,717 (6,619) controls, 578 (654) rubella, 103 (139) measles, 298 (353) chickenpox, 501 (565) mumps and 33 (34) poliomyelitis. Most of the losses were due to cases found to be either wrongly included, moved to unknown addresses or refused examination. The numbers who refused examination were 211 controls, 23 rubella, 6 measles, 15 chickenpox, 12 mumps and 1 poliomyelitis so that the refusal rate never exceeded 5%. The poliomyelitis data were too few for an informative comparison with the control series, but they are described in detail.

The 5,717 control pregnancies resulted in 92 (1·6%) abortions, 156 (2·7%) stillbirths and 5,469 (95·7%) live births. 93% of the mothers had children surviving to age 2 years and 385 (6·8%) of the live and stillbirths were premature (*i.e.* birth weight 5½ lb. or less). "Control" pregnancies were selected early in pregnancy (usually at mother's first visit to a doctor or midwife). "Virus"

pregnancies were selected at any stage of pregnancy determined by the time of the illness. As the period of observation (*i.e.* from time of selection) had a bearing on the outcome (*e.g.* on the proportion of miscarriages or premature infants observed in a series of pregnancies), the observed percentage of "virus" pregnancies with a given outcome (*i.e.* abortion, stillbirth, premature births, infant deaths, congenitally malformed infants, etc.) were compared with those expected from the "control" pregnancies after standardization of the latter for the period of risk.

The observed percentages, with those expected in brackets, for each type of outcome of 578 pregnancies complicated by rubella were: abortions 1·9 (1·2)%, stillbirths 3·5 (2·5)%, live birth 94·6 (96·3)%, deaths before age 2 years 4·2 (2·5)% and children surviving at age 2 years 90·4 (93·8)%. For cases in which the rubella occurred before the 13th week of pregnancy the differences were more marked; abortions, 5·0 (2·4)%, stillbirths, 4·5 (2·4)% and died before age 2 years, 6·9 (2·4)%, whereas for the cases where the virus infection occurred after the 13th week the percentages were 0·3 (0·5)%, 3·0 (2·6)% and 2·7 (2·6)% respectively. The infant mortality rate for 202 children whose mothers had rubella in the first 3 months of pregnancy was 76·5 per 1,000 live births (based on 14 infant deaths) compared with 43·9 per 1,000 (based on 24 infant deaths) in the whole "rubella" series and 25·8 per 1,000 in the controls. These results and more detailed analysis show that when rubella occurred in the first 12 weeks of pregnancy, the pregnancies so complicated ended with relatively more abortions, stillbirths, infant deaths, congenital malformations (particularly of the heart, eye and ear) and babies of low birth weight than did comparable pregnancies which were not complicated by a virus infection. At the medical examinations of live born children during their first two years of life major congenital defects were found in 2·3% of all live born children in the control series compared with 15·8% of those whose mothers had rubella before the 13th week of pregnancy and 2·2% of those whose mothers had rubella later in pregnancy. Of the series whose mothers had rubella in the first 3 months of pregnancy 4·7% (0·2% in controls) of the surviving children at age 2 had congenital heart disease, 4·7 (0.04)% had cataract, deafness was detected in 3·0 (0·08)% and suspected in 3·6 (0·4)%, mental defects were found in 1·8 (0·4)%, pyloric stenosis in 1·2 (0·2)% and intestinal atresia in 0·6 (nil)%.

The report deals fully and in a similar manner with each of the other types of "virus" pregnancies, but only measles gave any indication of an association between the virus infection in pregnancy and the foetal condition. The outcome of pregnancies complicated by chickenpox were (with the comparable control percentages in brackets): abortions 1·3 (0·8)%, stillbirths 1·7 (2·6)% and deaths under age 2 years 2·7 (2·5)%. The corresponding proportions for pregnancies complicated by mumps were: abortions 1·0 (0·8)%, stillbirths 1·8 (2·6)% and deaths under age 2 years 2·4 (2·5)%. For the mothers attacked by measles during pregnancy the proportions were: abortions 1·9 (1·0)%, stillbirths 1·9 (2·7)% and deaths under age 2 years 7·8 (2·3)%; when only attacks of measles in the first 12 weeks of pregnancy were considered the percentages were: 2·7 (1·9), 2·7 (2·7) and 16·2 (2·4)% respectively, so that the higher infant death rate, and a slightly higher proportion of malformed children also noted, requires further examination. Specially collected data relating to influenza during 166 pregnancies in Manchester and Liverpool in 1951 resulted in corresponding proportions of: abortions 0·6 (1·0)%, stillbirths 1·2 (2·7)% and deaths under age 2 years 3·6 (2·5)%. This high infant death rate was largely restricted to 99 mothers who had influenza between the 13th and 28th weeks, but "it is considered unlikely that this was due to the occurrence of influenza".

57 children whose mothers had rubella in the first 18 weeks of pregnancy and who lived in the London area were examined at ages 3–5 and compared with 57 children of similar age and sex. This re-examination showed a much higher prevalence of impaired hearing than that found or suspected at 2 years of age, so the survey was extended to all parts of the country with the result that an estimate of 19% for the live born surviving children of mothers who had rubella in the first 12 weeks of pregnancy is proposed—however, only in about 33% of the deaf was the handicap severe.

[The results of this enquiry are set out in great detail with notes on individual deaths and malformations so that it provides a wealth of clinical and statistical detail. The appendices set out distributions which can only be summarily treated in the text.] *E. A. Cheeseman*

WILSON, D. R., LENKEI, S. C. & PATERSON, J. F. **Acute Constrictive Epicarditis following Mononucleosis. Case Report.** *Circulation.* New York. 1961, Feb., v. 23, No. 2, 257–60, 7 figs.

RUBINI, M. E., JABLON, S. & MCDOWELL, M. E. **Renal Residuals of Acute Epidemic Hemorrhagic Fever.** *Arch. Intern. Med.* 1960, Sept., v. 106, No. 3, 378–87. [21 refs.]

This paper records some of the findings relating to renal damage in 1,416 white men serving in the U.S. forces who had epidemic haemorrhagic fever (EHF) in Korea between January 1951 and August 1953, and it also records follow-up studies for evidence of renal disease in these patients up to the end of August 1956. The report is from the Department of Metabolism, Division of Medicine, Walter Reed Army Institute of Research, Walter Reed Army Medical Centre, and the Follow-Up Agency, National Research Council, Washington D.C.

The first part of the study involved scrutiny of case records, and from these a tabulation is made of all cases of EHF and of those classified as moderate and severe. Proteinuria was present in all, and oliguria was common. In over 40% the urine output fell below 500 ml. per day. In nearly all cases the blood urea nitrogen level was raised. The findings suggest acute renal damage followed in most by rapid recovery.

By comparing the follow-up study of former EHF sufferers with controls it was apparent that the former EHF patients attended hospital much more often for some disease of the urinary system than did the controls. Moreover, those formerly classified as severe EHF cases had about 4 times as many admissions to hospital for urinary disorders as did those classified as mild cases. The commonest finding was a defect in the power of concentrating

the urine. In 2 cases a proved infection of the urinary tract was present while in 15 others the records suggest that this was the cause of admission to hospital.

A clinical study of 15 subjects was possible and case records of 9 of these are presented in detail. There was some evidence of depression of renal tubular function. It is concluded that while most patients with EHF recovered completely some must have lost their reserve of renal function, and this predisposes them to further urinary disorders. *S. Bell*

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

POSTGATE, J. R., CRUMPTON, Janet E. & HUNTER, J. R. **The Measurement of Bacterial Viabilities by Slide Culture.** *J. General Microbiol.* 1961, Jan., v. 24, No. 1, 15–24, 3 figs. & 2 pls. [18 refs.]

Many procedures have been described for estimating the proportion of viable to dead micro-organisms in a culture. The aim has usually been to increase accuracy, or to simplify manipulations, or both. This paper describes a fairly simple technique applicable to aerobic bacteria, yeasts and spore suspensions involving little in the way of special equipment.

A thin layer of nutrient agar is placed inside a 1 mm. deep annular ring on a microscope slide. The inoculum, consisting of a small quantity of a suspension containing about 100×10^6 cells/ml., is spread over the surface of the agar, and the ring is sealed with a cover-slip. The slide is incubated for long enough to allow several divisions of viable cells to occur and then examined by phase contrast microscopy. The numbers of non-dividing cells and of micro-colonies are counted in each of 10 fields.

The method gives a variation in estimation with 95% fiducial limits of ± 9% compared with a variation of about ± 13% in total counts done with a 0·03 mm. deep Thoma chamber. In estimating the proportion of viable cells by coupling a plating-out procedure with a direct count the variations due to the plating out procedure would, of course, increase this figure of 13%.

Various applications of the method to determine the proportion of a population killed by a bactericide are described. *R. B. Morrison*

GODINGER, D., SHARON, N. & OLITZKI, A. L. **Determination of Viable Counts of Bacterial Suspensions of Low Density by the Aid of Photometry.** *Bull. Res. Counc. of Israel.* 1960, Nov., v. 8E, No. 4, 157–61, 4 figs.

KOKKO, U. P., STUART, J. & TAYLOR, G. **Mailing of Infectious Specimens for Diagnostic Purposes.** *Pub. Health Rep.* Wash. 1960, Nov., v. 75, No. 11, 979–84, 5 figs.

The postal regulations governing the dispatch of pathological material by letter post to recognized laboratories for examination are much the same in the United States of America as they are in Great Britain. They are mainly designed to safeguard those handling such packets from risk of infection and to ensure that they contain a sufficiency of suitable packing material to absorb any fluid which may escape from the inner container under any conditions. This paper describes a recommended method of packing such pathological or infectious material for transmission by post. The specimen, itself, is placed either in a glass-sealed container, or a properly sealed rubber-stoppered glass bottle or tube, and surrounded by an adequate amount of absorbent packing material, placed in a can of suitable size with a properly fitting press-on lid which is finally enclosed in a cardboard carton for dispatch by letter post. Tests of resistance of the containers are described.

[The recommended design is by no means novel. It is very similar to the one in common use in Great Britain more than 50 years ago which was supplied by private laboratories to all who wished to send them specimens for examination. At that time, apart from patients in hospitals with bacteriological laboratories, almost all bacteriological diagnostic work was sent to distant laboratories through the post. The same applied to a great deal of other clinical pathological work and there were postal-containers for most types of specimens which conformed to the Post Office Regulations of Great Britain; the majority of these postal-containers were of similar construction to those described in this paper.] *H. J. Bensted*

RILEY, I. H. & WINNER, H. I. **A Note on Bacteriological Toxicity Tests of Silicone Rubbers for Medical and Pharmaceutical Uses.** *J. Pharmacy & Pharmacol.* London. 1961, Feb., v. 13, No. 2, 111–14.

Silicone rubbers which have found their uses in medicine and pharmacy in transfusion tubes, drainage tubes, baby bottle teats, and pharmaceutical vial stoppers are usually found to consist of polydimethyl siloxane polymer and a fine particle size filler, usually fume silica. To confer elasticity on these materials curing agents which form a cross-linked structure between polymer and filler, and are mainly organic peroxides such as benzoyl peroxide, are incorporated. Decomposition products of these curing agents have in the past been considered responsible for toxic properties and it was thought necessary to remove them by a curing process usually involving exposure to air at 250°C. for up to 24 hours. Shorter cures would, however, be desirable to preserve certain physical properties, such as tear strength.

The presence of unsaturated vinyl groups in the siloxane polymer allows a wider range of curing agents to be employed and newer agents such as dicumyl peroxide and di-tertiary-butyl peroxide as well as the more commonly used 2,4-dichlorobenzoyl peroxide were investigated for possible toxic properties in varying states of cure in these studies.

Standard toxicity tests for silicone rubbers used for transfusion purposes are based on the demonstration of inhibition by the rubber of the growth of a single species of *Streptococcus pyogenes.* The authors tested a wider range of bacteria including *Str. pyogenes, Staphylococcus pyogenes, Escherichia coli, Pseudomonas pyocyanea, Pneumococcus* sp. and *Streptococcus viridans* in estimating the toxicity of various rubber formulations in varying states of cure.

With these methods it was shown that most silicone rubbers have a very low toxicity. Two proprietary rubbers tested, Silastomer 156 and DP. 2452 (Midland Silicones Ltd.) would not have passed the standard test for transfusion rubbers, and formulation with di-tertiary-butyl peroxide caused slight inhibition of *Str. viridans.* Rubber formulations with polymethyl vinyl siloxane polymer and fume silica base with either 2,4-dichlorobenzoyl peroxide or dicumyl peroxide as curing agents were free of toxic properties regardless of the state of cure, and were recommended for the most stringent applications in medicine and pharmacy.

Frederick D. Lee

HOLLAND, P. D. J. **Report of a Hospital Trial of the Bactericidal Effect of a Hexylresorcinol Aerosol.** *Irish J. Med. Sci.* 1961, Jan., 6th Ser., No. 421, 31–7.

"Aerovap" vaporizers distributing hexyl resorcinol were installed in the corridor of a cubicle ward for children. The numbers of airborne bacteria were estimated by means of a slit sampler. Samples taken before the vaporization started gave total bacterial counts of 42 and 40 colonies per cu. ft.; samples taken after 7, 9 and 14 days' continuous vaporization gave counts between 0 and 11 colonies per cu. ft. [The tests reported as indicating absence of inhibition by hexyl resorcinol on the sample plates are not very convincing.] Counts within the cubicles were extremely variable but are claimed to show a significant reduction. The numbers of *Staphylococcus pyogenes* in floor dust also appeared to be reduced. *R. E. O. Williams*

STEINGOLD, L. & ASHWORTH, L. **Recirculation with Electrostatic Filtration as a means of reducing Bacterial Air Contamination.** *J. Applied Bact.* 1960, Apr., v. 23, No. 1, 120–24, 4 figs.

Tests were made with a small electrostatic precipitator in an air recirculator (Harris Trion Engineering Co. Ltd.), in a single-bed cubicle, an isolation ward and a surgical dressing cubicle. [The volume of air recirculated is not given.] During its use the count of airborne bacteria was very greatly reduced, especially in respect of the peaks associated with bed making and other activities. [The initial cost of an electrostatic precipitator is necessarily high. The same degree of air cleansing can be obtained with fabric filters, although the fan will need to be more powerful and therefore often somewhat noisier.] *R. E. O. Williams*

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; other Therapeutic Substances; Disinfection.**

BROWN, J. R., BECK, R. W., WOODWARD, J. M. & PORTER, R. P. **A Rapid Test for Bacterial Sensitivity to Antibiotics.** *Amer. J. Clin. Path.* 1961, Jan., v. 35, No. 1, 10–13, 1 fig.

The apparatus used for this test looks like a paint box, in which each of 28 shallow troughs contains a piece of blotting paper impregnated with bacterial nutrients, a tetrazolium salt, and an antibiotic. Each of these is inoculated with 2 or 3 drops of the test material: this can be either a broth culture or the clinical specimen itself (*e.g.* urine). Other types of specimen "require inoculation into a suitable broth culture medium", which need rarely be incubated for more

than 12 hours and often only 2–6 before being used as the inoculum. Bacterial growth on the paper reduces the tetrazolium salt, producing a red colour, indicating non-susceptibility to the antibiotic in the amount present. The test itself can be read in 2–6 hours, the control being a paper containing no antibiotic. [The 2 objections to such a method, of which this is not the first to be described, are that some important bacteria will not grow at all on such a contrivance, and that if actual specimens or impure cultures are used, the growth of an indifferent organism and not that causing the infection, may determine the result observed. This should obviously be always confirmed later with a pure culture, a precaution on which the authors do not very strongly insist, though they do remark that " Accurate evaluation of specimens for susceptibility to the testing of antibiotics must be done with pure cultures ".]

L. P. Garrod

Ritzmann, S. E. & Levin, W. C. **Effect of Nitrogen Mustard upon Antibiotic Activity of Penicillin, Erythromycin and Chlortetracycline.** *Texas Reports on Biol. & Med.* 1960, v. 18, No. 4, 646–53, 1 fig. [12 refs.]

Added to penicillin solutions in a *Sarcina lutea* cylinder plate assay, nitrogen mustard causes a moderate but significant reduction in the width of the inhibition zones produced. There is no such effect on erythromycin or chlortetracycline. The authors suggest that in patients treated with both nitrogen mustard and penicillin the effect of the latter may be impaired [although in fact the lowest concentration of nitrogen mustard shown to have this effect was 13 times greater than that likely to be attained in the blood immediately after a conventional dose].

L. P. Garrod

Gillissen, G. & Heusel, E. Zur Kritik der Sterilitätsprüfung penicillinhaltiger Präparate. [**Observations on the Testing of Penicillin Preparations for Sterility**] *Arch. f. Hyg. u. Bakt.* 1961, Feb., v. 145, No. 1, 32–43. [23 refs.]

A sterility test of penicillin can be performed either by passing a solution through a membrane filter, which is then cultivated, or by cultivating the solution itself after inactivating the penicillin in it. A drawback of the second method is that if the contaminating bacteria are penicillin-sensitive, they may be killed during any slow process of inactivation. Of the inactivating substances used for this purpose, cysteine, penicillinase and hydroxylamine hydrochloride, the authors have examined the last-named, and demonstrated another drawback, namely, that the inactivator itself may be bactericidal. They tested the action of hydroxylamine hydrochloride on *Staphylococcus aureus, Streptococcus pyogenes, Escherichia coli, Bacillus subtilis, Clostridium tetani* and 5 varieties of fungi with regard to both bacteriostatic and bactericidal action. The results are difficult to understand because of insufficiently explanatory headings to the tables, but the authors have satisfied themselves that most of these organisms (exceptions being bakers' yeast and " pathogenic yeasts ", which were much more resistant) might be killed under the conditions of the test by a hydroxylamine hydrochloride concentration of 0·33%, which is required to inactivate penicillin in a concentration of 10^4 units per ml. Were the penicillin concentration higher, an additional source of error might be incomplete inactivation.

L. P. Garrod

Leyh-Bouille, Mélina. Influence de la nature de milieu sur la conversion en sphéroplastes par la pénicilline de mutants auxotrophes d'*Escherichia coli*. [**Influence of the Nature of the Medium on the Conversion of Autotrophic Mutants of *Escherichia coli* into Spheroplasts**] *C.R. Soc. Biol.* 1960, v. 154, No. 7, 1500–502. [Refs. in footnotes.]

It is usually believed that the formation of spheroplasts from bacterial cells exposed to penicillin can only occur in a medium permitting growth, but there is a report of this change in *Staphylococcus aureus* in a non-nutrient medium. The present author finds that this is not true of a strain of *Escherichia coli*. The parent culture formed spheroplasts in the presence of penicillin in a medium consisting of salts and glucose only when ammonium sulphate was added, and mutants requiring proline, tryptophan and arginine formed them only when these nutrients were also provided. *L. P. Garrod*

Hugo, W. B. & Russell, A. D. **Action of 6-Aminopenicillanic Acid on Gram-Negative Bacteria.** [Correspondence.] *Nature.* 1960, Dec. 3, v. 188, 875.

Although 6-aminopenicillanic acid is credited with only a low degree of antibacterial activity, these authors have found that it is nearly as active as benzyl penicillin in inducing spheroplast formation in *Escherichia coli* and 5 other species of Gram-negative bacilli.

L. P. Garrod

Kneebone, G. M. & Maxwell, G. M. **6(Alpha-Phenoxyproprionamido) Penicillanic Acid Potassium Salt: Studies in the Paediatric Age Group.** *Med. J. Australia.* 1960, Dec. 24, v. 2, No. 26, 1002–5, 1 fig.

These authors from Adelaide gave a single dose of phenethicillin (Broxil) to 25 children and assayed the antibiotic in the blood after 1, 2, 4 and 6 hours. The dose was 250 mgm. for children aged 5–12 years and 125 mgm. for those under 5, including some aged only a few months (3 of these received 62·5 mgm.). The levels found were very variable (from 0·96 to 12·8 μgm./ml. at 1 hour and from (apparently) nil to 6·52 at 2 hours) but they are regarded as corresponding to those found by others in adults [this *Bulletin*, 1960, v. 35, 383] and as higher than those obtainable with the same dose of penicillin V. No relationship was evident between the blood level attained and the ratio of the dose to either body weight or surface area. [Surely such a relationship must exist? It is presumably

obscured here by the operation of other factors accounting for the large variations observed.] In other experiments it was found that no antibiotic was detectable in the cerebrospinal fluid of 3 children given 250 mgm. 1 hour before lumbar puncture, and that when 500 mgm. was given to women in a late stage of labour, the antibiotic was present in the cord blood in concentrations approaching those in the maternal. *L. P. Garrod*

BRANCH, A., RODGER, K. C., LEE, R. W. & POWER, Edna E. **Clinical and Laboratory Experiences with a New Synthetic Penicillin—2,6-Dimethoxyphenyl Penicillin.** *Canadian Med. Ass. J.* 1960, Nov. 5, v. 83, No. 19, 991–6, 1 fig. [32 refs.]

Tests by a tube dilution method of 35 strains of staphylococci showed varying degrees of resistance to penicillin G and corresponding but lesser degrees of resistance to phenethicillin, but uniform sensitivity to 2,6-dimethoxyphenyl penicillin (methicillin, Staphcillin in America, Celbenin in Great Britain), the inhibitory concentration being with few exceptions (these being 1 tube above or below) 1·56 μgm./ml. Methicillin was given intramuscularly in doses of 0·5 or 1 gm. at 4-hour intervals to 12 patients with staphylococcal infections: 9 of the 12 strains of staphylococci were resistant to penicillin G. Brief case-histories are given: 3 patients had pneumonia, 1 acute bronchitis, 4 boils or carbuncles, 2 abscess or wound infection, 1 urethritis and conjunctivitis, and 1 osteomyelitis complicating plated fracture of the femur and Paget's disease. All responded satisfactorily except the last-named. Various tests having reference to hepatic and renal function gave normal results. Observations were made on the levels of methicillin in the blood (but there is no key to the 6 lines in the graph giving the results). *L. P. Garrod*

(i) FISK, G. C. **Respiratory Paralysis after a Large Dose of Streptomycin. Report of a Case.** *Brit. Med. J.* 1961, Feb. 25, 556–7. [11 refs.]

(ii) BUSH, G. H. **Prolonged Neuromuscular Block due to Intraperitoneal Streptomycin.** [Memoranda.] *Brit. Med. J.* 1961, Feb. 25, 557–8. [11 refs.]

These papers, respectively from Guy's Hospital, London, and Alder Hey Children's Hospital, Liverpool, report single cases in which apnoea followed the introduction of large amounts of streptomycin into an operative area before closure of the wound. Streptomycin, and still more neomycin, is known to have a neuromuscular blocking action, reversible by neostigmine, when given in large doses [this *Bulletin*, 1959, v. 34, 1154]. Fisk's patient was a man of 53 with an oesophageal stricture which was repaired with a jejunal transplant in an operation lasting 7 hours, at the end of which 10 gm. streptomycin powder was introduced, 5 gm. each into the pleural and peritoneal cavities. The second patient was an infant aged 6 months who had a hemicolectomy for Hirschsprung's disease: at the end of the operation 1 gm. of streptomycin was "inadvertently" instilled into the peritoneal cavity. In both cases D-tubocurarine had been used, but since in both spontaneous respiration had been resumed before the end of the operation it is concluded that the apnoea which followed must have been due to, or at least contributed to, by the streptomycin. Both patients recovered after several hours of continued artificial ventilation and treatment with atropine, neostigmine and other drugs. *L. P. Garrod*

KAVELMAN, D. A. **Streptomycin and Acute Anaphylaxis.** *Canadian Med. Ass. J.* 1961, Feb. 11, v. 84, No. 6, 332–3.

"Anaphylaxis to streptomycin, although far more rare than that due to the administration of penicillin, can and does occur. A presumed case of this entity is presented. Anaphylaxis appeared after the eighth 12-hourly dose of streptomycin and was characterized by agitated shock and massive fecal urgency productive of blood in the stool, presumably due to trauma. This patient was treated with intermittent intravenous metaraminol to maintain the blood pressure for the first six hours, after which the patient rapidly improved to regain his normal state within 24 hours. Extensive laboratory investigation over the ensuing three weeks disclosed only a mild defect in the concentrating ability of the kidney, and a rare granular cast seen on one of ten microscopic examinations of the urine. Not only penicillin, but *any* of the antibiotics, can cause anaphylactic reactions, and physicians must be prepared to treat these reactions should they occur."

OTTE, H. J. Gewebsspiegelbestimmungen nach intravenöser Tetracyclinapplikation. [**Determination of Tetracycline Tissue Concentrations after Intravenous Administration**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 569–81, 8 figs. [35 refs.]

A single intravenous dose of pyrrolidinomethyltetracycline (PMT) or of oxytetracycline (O) (this apparently in a special form for this method of administration) was given to rabbits: the dose of each was 14·4 mgm./kgm., this being the equivalent to 250 mgm. to a man of 70 kgm. PMT was well tolerated but the injection of O apparently caused severe pain. The rabbits, of which 100 were used in all, were exsanguinated at intervals of 5, 15, 30, 60, 120, 240 and 360 minutes after injection, and the antibiotic was assayed in the serum and bile, and in homogenates of heart, lung, liver, spleen, and kidney, the *Bacillus cereus* cup (hole) plate method being used. The results are presented both in tables and graphically, the latter distinguishing between bacteriostatic and (>25 μgm./ml.) bactericidal concentrations.

The main features of organ distribution of both antibiotics were the very low concentrations in the brain, concentrations in the heart and lungs somewhat lower than those in the blood, and in other organs exceeding those in the blood. With one exception the concentration of PMT exceeded that of O in every organ and fluid at every time interval, the difference usually being considerable. The exception was kidney, in which O

reached a very high peak concentration of 239 μgm./gm. in 5 minutes, whereas PMT reached its peak after 1 hour (128 μgm./gm.). It seems therefore that O is very rapidly excreted by the kidney, and this accounts for the lower concentrations found elsewhere throughout. PMT reached a much higher concentration in the bile (maximum 85 μgm./ml.) than O (13 μgm./ml.) each peak being at 2 hours. It is concluded that PMT is the more suitable of these forms of tetracycline for intravenous use. *L. P. Garrod*

CRONK, G. A., BUCKWALTER, F. H., WHEATLEY, W. B. & ALBRIGHT, H. **The Absorption and Excretion of N-(Pyrrolidinomethyl) Tetracycline.** *Amer. J. Med. Sci.* 1961, Jan., v. 241, No. 1, 1–13, 8 figs.

This paper from the Department of Health and Preventive Medicine, Syracuse University and the Bristol Laboratories, Syracuse, New York, reports the results of blood and urine assays in groups of 5 or 10 normal adults following single or repeated intramuscular injections of N-(pyrrolidinomethyl) tetracycline. Each "vial" of the antibiotic (quantity of this is not stated) also contained 300 mgm. of ascorbic acid and 40 mgm. of lignocaine: when the latter was omitted there was immediate and apparently rather severe pain at the injection site, but when it was included the onset of pain was delayed and it was less severe. The single doses given varied from 143 to 786 mgm. and doses repeated at intervals of 8, 12 or 24 hours from 178 to 393 mgm. The results are presented in both tables and graphs, and may be summarized by saying that adequate therapeutic levels can be consistently maintained in the blood by moderate dosage. Excretion is slow, the percentage of the dose appearing in the urine during successive 6-hour periods up to 30 hours being 20, 13, 8, 8 and 5: other evidence of this is provided by the fact that 24 hours after the highest single dose the average blood concentration is still 1·79 μgm./ml. Some cumulative effect was observed when repeated doses were given at 8- or 12-hour intervals. [Higher and more consistent blood levels can evidently be achieved with this form of tetracycline than with the same dose of this antibiotic in its ordinary form given orally, but this study includes no comparative trials by the oral route to prove this.] *L. P. Garrod*

MUKAI, F. H. **Interrelationship between Colicin Sensitivity and Phage Resistance.** *J. General Microbiol.* 1960, Dec., v. 23, No 3, 539–51, 4 figs. [Numerous refs.]

Escherichia coli 15 can be induced by UV irradiation to produce colicine 15, to which it is itself sensitive. It was found that most colicine was produced in those cultures in which most growth had occurred before lysis. Colicine appeared to be synthesized in bacteria which elongated during the growth period and which later lysed to release it. Many bacteria survived in induced cultures and were therefore resistant to colicine 15, but the resistance was only transitory. When these organisms were recovered and tested for sensitivity to colicine, they were as sensitive as organisms from unirradiated cultures.

However, 2 mutants with a heritable resistance to colicine 15 were also isolated. Both were found to be sensitive to infection by all the T phages, whereas the colicine-sensitive parent was resistant to all except T2. A series of 1-step mutants resistant to each T phage were selected from the 2 colicine-resistant mutants, but none had lost its resistance to colicine. When further mutants resistant to more than 1 phage were selected from the 1-step mutants, it was found that they still retained their resistance to colicine 15 except some which were resistant to at least T1, T3, T4, T5 and T7 (presence or absence of T6 sensitivity did not matter) which had become sensitive to colicine 15. Not all the mutants obtained which were resistant to the 5 phages were sensitive to colicine but the only ones sensitive to colicine were resistant to the 5 phages.

The relationship between sensitivity to colicine and to phages has been described previously, *e.g.* FRÉDERICQ and GRATIA [this *Bulletin*, 1951, v. 26, 80] who found that colicine K and phage T6 shared the same receptor. By contrast, the relationship described here is inverse, in that phage sensitivity accompanies colicine resistance. A diagram is given depicting possible changes by which receptor sites for colicine 15 could be acquired at the same time as resistance to the 5 T phages.

Janice Taverne

BRACKEN, A., WILTON-DAVIES, C. C. & WEALE, F. E. **Ethylene Oxide Serilization of a Heart-Lung Machine.** With a **Bacteriological Note** by J. C. KELSEY. *Guy's Hosp. Rep.* 1960, v. 109, No. 1, 75–80, 1 fig.

The authors describe a method for sterilizing a Mark-Gibbon heart-lung machine, which consists of several Perspex boxes, stainless steel oxygenation screens and tubing made of plastic and rubber. It was desirable to sterilize the machine assembled because of its complexity. Early experiments in which the entire system was perfused with hot water at 95°C. were successful in producing wash fluids free from vegetative organisms but the method was discarded for fear of warping the plastic components. It was then decided to use a mixture of 10% ethylene oxide with 90% carbon dioxide in a plastic bag. A large bag of PVC [polyvinyl chloride] was designed which would contain the parts of the machine which needed sterilizing wrapped in cloth in their assembled state. The gas mixture was led from a cylinder, through a heating coil immersed in hot water to prevent frosting, and thence into the bag by two plastic tubes. These were connected inside the bag to the arterial and venous leads in such a way that gas had to pass through all parts of the system before escaping into the bag.

The complete process consisted of the evacuating of the bag until it was fully collapsed, and running in the gas mixture until it was fully distended. Evacuation and filling were repeated, the tubes were occluded and the bag left at room temperature for 24 hours. After 12 hours some "topping up" was sometimes needed to replace losses from leakage. At the end of 24 hours the system was freed from gas by alternate evacuation

and inflation with nitrogen and finally flushed through with a slow stream of nitrogen overnight. The system was checked by using paper discs containing 10^5 spores of *Bacillus sterothermophilus*. In all of 19 cultures exposed on 5 occasions the spores were killed. The process is in routine use and the authors state that no ill effects have been discovered. They hope to introduce further simplifications later.

[This work was done before it was realized that spores dried on to paper are easier to kill than those dried on to plastic, metal or glass. The *globigii* strain of *Bacillus subtilis* would have been a better test organism to use. The kill of such a resistant organism would probably be less than that of 10^5 here reported. Since the apparatus must be scrupulously clean before sterilization the lower efficiency can probably be taken as still adequate.]

J. C. Kelsey

THOMAS, J. A. Méthode de stérilisation bactériologique et de désinfection sans surpression par l'action synergique ménagée et brève de l'oxyde d'éthylène puis de l'ozone. [**A Short and Simple Method of Bacteriological Sterilization and Disinfection by the Successive Action of Ethylene Oxide and Ozone**] *Bull. Acad. Nat. Méd.* 1960, v. 144, No. 35, 835–8.

The author was faced with the problem of sterilizing the plastic components of a heart-lung machine. Ethylene oxide was found to be slow and to damage certain plastics, notably polyvinyl chloride: ozone was uncertain in its action. The two agents used together proved more effective than either alone. A stainless steel gas-tight vessel of 100 litres capacity was used. The humidity was controlled by the presence of a pot of water, and a fan was used to circulate the gases. The temperature was maintained at about 40°C.

First ethylene oxide was admitted to a concentration of 100 mgm. per litre—after an exposure of 30 minutes the chamber was flushed through with a continuous current of ozonized oxygen for a further period of 30 minutes. The emerging gas was passed through solutions to absorb the ozone. No vacua were drawn. As a third sterilizing measure an ultra-violet light was fitted inside the chamber.

This combination of processes did not damage the plastic equipment. The sterilizing efficiency was tested by spreading drops of broth cultures of various organisms either upon glass strips or directly onto surgical instruments. These test objects were subjected to the sterilizing processes before the broth had evaporated, and were subsequently cultured in broth. A number of strains of bacteria were used including *Staphylococcus aureus* and *Bacillus subtilis*. It is not stated whether vegetative forms or spores of the latter were used.

The author concludes that his method is effective, of wide application, safe and simple.

[It is hard to share this opinion—the bacterial challenge used to test the method was highly artificial, and probably not very exacting: also the method can hardly be described as simple. It is probable that the future development of plastics will produce materials that resist ethylene oxide and possibly high temperatures also. For a method of sterilizing a heart-lung machine which, though slower, is effective and relatively simple, see BRACKEN *et al.*, above.] *J. C. Kelsey*

GILLISSEN, G. & SCHOLZ, H. G. Untersuchungen zur Abtötung von Milzbrandbazillen und deren Sporen. [**Investigations on the Killing of Anthrax Bacilli and Spores**] *Desinfektion u. Gesundheitswesen.* 1960, Oct., v. 52, No. 10, 140–44. [35 refs.]

The substance investigated was β-propriolactone.

The considerable periods of exposure to solutions necessary to kill the bacilli and their spores on the one hand and the failure of sterilization of hides exposed to an aerosol of this substance on the other show that it is not a specially useful antiseptic for treatment of hides and hair infected with anthrax. *J. W. McLeod*

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

REIMANN, H. A. **Variation of *Staphylococcus (Micrococcus Pyogenes)*.** *Arch. Intern. Med.* 1960, Sept., v. 106, No. 3, 341–4, 4 figs.

Staph. aureus PC1 209P phage type 42D was left to age in broth or on agar plates at room temperature. Segments of colonies were subcultured to agar plates and resulting colonies were of 9 different colonial types; mucoid (M), smooth (S) or rough (R) colonies each of which could be white (W), yellow (Y) or buff (B) (see Reimann, *Proc. Soc. Exper. Biol. & Med.*, 1957, v. 96, 411). It is not clear how stable these variants were but change from Y to W was common and R colonies were less stable than M or S variants.

All Y and B variants and the RW colonial form were of the same phage pattern (42D), MW was weakly lysed by phage 42D and SW was lysed by 18 other phages but not by phage 42D.

After 18 transfers in a subinhibitive concentration of penicillin, SY cocci showed an increased resistance from 0·02 units/ml. to 0·25 u./ml. SW cocci showed an increased resistance from 0·015 u./ml. to 0·12 u./ml. after 9 transfers. Colonial morphology of the 2 types was unchanged but the individual cocci appeared larger.

All Y and W variants and the MB form were injected subcutaneously, in melted agar, into mice and the resulting masses were aspirated at intervals of several days. Up to 8 days all forms except SW grew heavily. At 8 days variants were unchanged in colonial morphology except for a few MY colonies from the MW focus and some MW colonies from the SY focus. Subcultures from RY infected sites grew as MY colonies and from RW sites grew as MB colonies. Subcultures from MB infected sites grew colonies of the same morphology. All mice survived. Some virulence tests were done but mice and rabbits were not killed by the variants under the conditions of the test. [It would be interesting to know if these variants differed in their production of coagulase, haemolysins or other toxins.]

M. Patricia Jevons

Bortolini, G. & Checchi, E. Variabilità dei più comuni tests per la patogenicità dello stafilococco in successivi controlli. [**The Variability Observed in Repeated Examinations of the More Commonly Used Tests for Staphylococcus**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, Oct., v. 41, No. 10, 545–54. English summary.

The tests used were those for coagulase activity, haemolysin, phosphatase, fibrinolysin, proteolysis (liquefaction of gelatin), fermentation of mannite and the biological test for enterotoxin in kittens. Repeated tests were made on 4 occasions, or with one or two of the tests less frequently, at intervals of about one or two months. A fluctuation from positive to negative results was repeatedly observed in all the tests and even with the coagulase test 19 out of 47 strains tested showed irregularities on repetition of the test.

The general conclusion is, therefore, drawn that no single laboratory test at present in use is a reliable guide to pathogenicity of staphylococcal strains.

J. W. McLeod

Karska, B., Kozak, W., Narbutowicz, B. & Stolarska, A. **The Lysogenicity of Staphylococci isolated in Poland.** *J. General Microbiol.* 1960, Dec., v. 23, No. 3, 577–81. [13 refs.]

The "lysogenicity pattern" of various staphylococci was determined. 122 coagulase-positive strains isolated from lesions and 65 coagulase-negative strains from lesions and other material from children in a hospital in Warsaw were investigated. A broth culture of the strain was induced by ultra violet light. After 24 hours in the dark at 4°C. the culture was centrifuged and the supernatant fluid spotted onto indicator strains consisting of the 20 propagating strains of the typing phages and 13 strains from the author's collection. Coagulase-negative strains were also tested on 35 coagulase-negative indicator strains. Strains not shown to be lysogenic by this method were cross-cultured [Fisk, this *Bulletin*, 1943, v. 18, 415]; the lysogenicity pattern of a strain was designated by a list of the propagating strains lysed by the liberated phage.

No phages could be detected in the supernatants of the 65 coagulase-negative strains after induction. The 122 coagulase-positive strains consisted of 57 belonging to phage group I, 19 to group I/II/III, 15 to group III, 4 to group II, 2 to group I/II, 1 to group II/III, and 25 were non-typable by the conventional typing method [this adds up to 123]. 93 of these strains released phage; 82 liberating phage detected on the standard propagating strains and 11 detected on strains from the author's collection. Thus 80% of strains could be classified by the usual phage typing method and 76% by their lysogenicity pattern. When both methods were used 92% could be classified and strains with a uniform typing pattern could be further subdivided on the basis of their lysogenicity pattern.

[No attempt was made to isolate the liberated phages by single plaque isolations to determine if the lysogenicity pattern was due to the action of one or several phages. Some staphylococci have been shown to carry as many as 5 phages.] *M. Patricia Jevons*

Rosenblum, E. D. & Jackson, J. L. W. **Lysogenic Conversion of Staphylococcal Strains of Type 80–81 and Related Phage Types.** *Texas Reports on Biol. & Med.* 1960, v. 18, No. 4, 654–61. [10 refs.]

The authors continue the studies of lysogenic conversion of staphylococci of type 80/81 reported by Asheshov and Rippon [this *Bulletin*, 1959, v. 34, 1175] and Rountree [*ibid.*, 1174].

79 strains of type 80/81 and related types (52/52A/80/81, 52/80, 29/52/52A/80/81, 42B/81) were tested for lysogenicity by cross-culturing and testing on 96 other indicator strains. The material included 6 paired cultures, each pair being from nose and throat of the same child, one of each pair being a type 80/81 strain and the other being a related type. None of the 80/81, only 1 strain of type 52/52A/80/81 and 3 of type 52/80 were found to be lysogenic.

A typical 80/81 strain and strains of the related typing patterns were then lysogenized with 4 phages: P53 from a strain of type 52/52A, P60 from a non-typable strain, P97 from a 52/80 strain and B-WM from a strain of type 52/52A/80/81.

Phages P97 and P53, which may be identical, were converting phages in that a type 80/81 strain after lysogenization became type 52/52A/80/81. Naturally occurring strains of type 52/52A/80/81 typed the same after lysogenization with these phages and the 80/81 strain was unaltered in typing pattern by lysogenization with phage B-Wm. Lysogenization of this strain with one of the converting phages rendered the strain sensitive to phage P60 and non-typable. Strains P97 and P59 of type 52/52A/80/81 were both non-typable after lysogenization with phage P60 although only strain P97 was demonstrably carrying a converting phage.

The low frequency of lysogeny among strains of type 52/52A/80/81 especially in the paired strains lead the authors to suggest that modification of the typing pattern is produced more often by mutation than by lysogenic conversion although they do not exclude this as a source of modified strains. Asheshov and Rippon however found that 33 of 39 strains of type 52/52A/80/81

carried converting phages and also showed that a lysogenic strain when cured retains its broader typing pattern. The authors reconcile these observations by postulating that the locus in the bacterial genome responsible for sensitivity to phages 52 and 52A is also the preferential site for attachment of the converting phages so that phage sensitivity may be altered either by mutation of that locus or by the nature of the attachment of the converting prophage to the locus.

M. Patricia Jevons

D'Arca Simonetti, A. Sulla fosfomonoesterasi del *Micrococcus pyogenes.* **[The Ferments of *Staphylococcus aureus* which Split Monophosphate Esters]** *Nuovi Ann. d'Igiene e Microbiol.* 1960, July–Aug., v. 11, No. 4, 303–14. [33 refs.] English summary.

The various techniques available for the investigation of hydrolysis by the phosphate esterases of bacteria are described and discussed.

The modification of Bray and King's method [this *Bulletin*, 1944, v. 19, 58] in which Ca monophosphate ester of phenol phthalein is suspended in a milk agar medium [*ibid.*, 1961, v. 36, 65] was found preferable to the use of Dorset's egg as in the original method. It was also superior to Schärer's method in which broth culture is added to buffered suspension of Na phenol phthalein phosphate and a bromo quinone is used to give a blue colour with the liberated phenol.

Among 512 strains of *Staphylococcus aureus* tested 323 gave a strong, 127 a moderate, and 61 a weak positive reaction. One strain at first negative was found weakly positive on repeated testing. The Schärer test gave 18 negative and 13 doubtful results with the same collection of staphylococci. *J. W. McLeod*

Oeding, P. **Antigenic Properties of *Staphylococcus aureus.*** *Bact. Reviews.* 1960, Dec., v. 24, No. 4, 374–96. [114 refs.]

In this useful review, Oeding, of the Gade Institute, Bergen, Norway, surveys first the earlier investigations of the immunological structure of staphylococci. Though several workers identified either protein or polysaccharide antigens, or both, there seems to have been singularly little attempt to correlate the different pieces of work. Recently there have been several studies of antigens showing cross-reactions with sera to various other groups of bacteria. Use has also been made of the red cell as a carrier for various antigens, and of agar precipitation. Although there are now some indications of the anatomical disposition of some antigens in the cocci, the main conclusion to be drawn from the first part of this review is that it is still impossible to present anything like a full account of the antigenic make-up of staphylococci in anatomical or chemical terms.

On the practical side, nevertheless, useful typing schemes have been devised, first by Cowan [this *Bulletin*, 1938, v. 13, 406; 1939, v. 14, 511] and latterly, and especially, by Oeding himself. It is useful to have an account of Oeding's work in one place, though the reviewer would like to have seen this section presented in greater detail for the original work is in many different papers. There is brief mention of studies attempting to correlate serological and phage typing, and of the epidemiological applications of the former.

R. E. O. Williams

Pereira, A. T. **Antigenic Loss Variation in *Staphylococcus aureus.*** *J. Path. & Bact.* 1961, Jan., v. 81, No. 1, 151–6.

Slide agglutination tests with absorbed sera prepared with 23 standard strains of staphylococci (Pereira, *Arquivos Inst. Bact. Camara Pestana*, 1961, v. 10, in press) were carried out on 883 recently isolated coagulase-positive strains from clinical lesions and nasal carriers. 86·5% were found to possess one or other of 5 antigens. 1, 3, 13, 17 or 18: 2·9% of them had more than 1. Antigens 13 and 17, however, were found to be unstable. The loss of antigen 13 after about 10 subcultures was accompanied by the appearance of antigen 3, and antigen 17 was replaced by antigen 1 after a variable number of subcultures. Old laboratory strains like the 13 international types [Hobbs, this *Bulletin*, 1949, v. 24, 87] tended to possess antigen 1 or 3. Changes in antigen pattern were not accompanied by changes in phage typing pattern. *M. Patricia Jevons*

Yotis, W. W. & Ekstedt, R. D. **Studies on Staphylococci. III. Further Studies on Purification and Mechanism of Action of an Antibacterial Human Serum Factor.** *J. Bacteriology.* 1960, Nov., v. 80, No. 5, 719–25, 5 figs.

The substance [this *Bulletin*, 1960, v. 35, 387] which inhibits growth and respiration of coagulase-negative staphylococci was shown to be present in a water-soluble globulin fraction of pooled human serum. When purified this globulin inhibited the respiration of resting cell suspensions of *Bacillus subtilis*, *Micrococcus lysodeikticus* and coagulase-positive and -negative staphylococci on glucose as substrate. Added coagulase protected the staphylococci and *B. subtilis* in this system. The antibacterial effect of the globulin could be demonstrated only when the cells were exposed in aqueous suspension or phosphate buffer below 10^{-4}M. Viability experiments showed a 90% reduction in viability of both coagulase-positive and -negative staphylococcal suspensions following exposure for 1 hour at 4°C. to 40 mgm./ml. of the globulin fraction. Pre-treatment of both suspensions with coagulase protected them against this lethal effect. Observation of globulin-treated staphylococcal suspensions in the electron microscope suggested that many of the cocci were undergoing lysis. Suspensions protected with coagulase showed no evidence of lysis.

H. Gooder

Goldner, M. & Wilson, R. J. **Preparation of Cell-Free Staphylococcal Penicillinase Concentrate.** *Canadian J. Microbiol.* Ottawa. 1961, Feb., v. 7, No. 1, 45–51, 3 figs. [14 refs.]

"The preparation of staphylococcal intracellular penicillinase as a cell-free concentrate is described and the

optimal conditions for its action on penicillin indicated. Cells were disrupted by sonic vibrations and the debris removed by centrifugation at 17000 × *g*. Cell-free concentrates were prepared from the supernatants and were found to have a higher activity per mg. nitrogen than the bacterial suspensions from which they were prepared. Centrifugation at 35000 × *g* resulted in a partial and as yet unaccountable loss of activity. The enzyme was optimally active at pH 6·0–6·5 and 30°C. The possible application of cell-free staphylococcal penicillinase to enzymatic and immunological work is discussed."

KÖHLER, W. & HEINRICH, H. Die Neomyzinempfindlichkeit der Staphylokokken. Zur Unterscheidung koagulasepositiver und -negativer Staphylokokken. [**Neomycin Sensitivity of Staphylococci. Differentiation of Coagulase-Positive and -Negative Staphylococci**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* 1960, Nov., v. 6, No. 11, 747–50.

These authors have verified a previous observation by GREER and MENARD (*Antibiotics Annual*, 1957–58, 149) that coagulase-negative staphylococci are more sensitive to neomycin than coagulase-positive. They examined 61 and 220 strains of each respectively by both a tube- and a plate-dilution method, the latter being found more satisfactory, and give the results as percentages of strains partially or totally inhibited by different concentrations of neomycin. There was some strain variation, but nevertheless little overlap between the range of concentrations inhibiting the 2 varieties of staphylococcus: of strains inhibited by 1 μgm./ml., 98·4% were coagulase-negative, and of those only inhibited by 2·5 μgm./ml. or more, 97·3% were coagulase-positive. 31 strains which were coagulase-positive in the tube test but negative in the slide test ("plasma agglutination") or vice versa were with 2 exceptions inhibited only by 2·5 μgm./ml. or more. Determination of neomycin sensitivity is suggested as an aid to the identification of strains of doubtful identity. [It does not distinguish between "coagulase-positive" and "-negative", as the title and text suggest, but may perhaps help to distinguish between 2 species, pathogenic and non-pathogenic. The difference in neomycin sensitivity being small, the conditions of any such test would need to be rigidly standardized. The authors suggest the use of a disc method, with a control culture of both varieties.]

L. P. Garrod

ROBERTS, W. S. L. & STEWART, F. S. **The Sugar Composition of Streptococcal Cell Walls and its relation to Haemagglutination Pattern.** *J. General Microbiol.* 1961, Feb., v. 24, No. 2, 253–60. [12 refs.]

"The sugar composition of cell walls of various streptococci and pneumococci was investigated by paper chromatography. Rhamnose was found in the walls of most streptococci bearing Lancefield group haptens but was not identified in the walls of pneumococci or most 'viridans' streptococci. In the group as a whole galactose and glucose were more regularly present than rhamnose. A significant correlation was found between the distribution of rhamnose and haemagglutination pattern, as determined by the presence of a widely distributed red cell sensitizing antigen and the production of an agent capable, like the receptor-destroying enzyme of the influenza virus, of modifying the antigenic properties of the red-cell surface."

ROBERSON, B. S., SCHWAB, J. H. & CROMARTIE, W. J. **Relation of Particle Size of C Polysaccharide Complexes of Group A Streptococci to Toxic Effects on Connective Tissue.** *J. Exper. Med.* 1960, Nov. 1, v. 112, No. 5, 751–64, 3 figs. [25 refs.]

The nature of the C polysaccharide complex, derived from Group A streptococci, which produces a chronic remittent and intermittent lesion of the dermal connective tissue of rabbits [this *Bulletin*, 1960, v. 35, 694] was further studied to establish the minimal unit possessing complete toxic activity. This activity was correlated with the rhamnose content of various particulate fractions produced by subjecting streptococcal cell walls to sonic vibration. Digestion of these fractions by proteolytic enzymes or ribonuclease and exhaustive chemical deproteinization failed to destroy activity. Activity was lost, however, when the toxic material was incubated with a *Streptomyces albus* culture filtrate. C polysaccharide hapten prepared from cell walls by formamide extraction was without toxic activity.

Fractions possessing the greatest toxic activity in terms of nitrogen content were prepared by sonic vibration of purified streptococcal cell walls, removal of the material sedimented by 11,500 *g* for 15 minutes and further centrifugation at 75,000 *g* for 60 minutes. The sediment obtained at this stage was treated with papain and further centrifuged in a discontinuous sucrose gradient. Active material was present throughout the gradient with the most active fraction distributed between sucrose densities of 1·10 and 1·15. These results are interpreted as suggesting that the maximum skin lesion activity is associated with C polysaccharide complexes intermediate in size between large cell wall fragments and group hapten.

H. Gooder

TAN, E. M., HACKEL, D. B. & KAPLAN, M. H. **Renal Tubular Lesions in Mice produced by Group A Streptococci grown in Intraperitoneal Diffusion Chambers.** *J. Infect. Dis.* 1961, Jan.–Feb., v. 108, No. 1, 107–12, 7 figs. [18 refs.]

BOYER, F. [Vaccination d'animaux de laboratoire avec des streptocoques. I. Avec des germes tués par la chaleur. II. Avec des germes virulents, vivants, sous protection d'antibiotiques. [**Immunization of Laboratory Animals with Streptococci. I. With Streptococci killed by Heat. II. With Living Virulent Streptococci under Protection by Antibiotics**] *Ann. Inst. Pasteur.* 1960, Dec., v. 99, No. 6, 897–904.

Groups of mice and rats were immunized intraperitoneally with a vaccine prepared from a mixture of heat-killed Group A and Group C streptococci or by

living Group A organisms. The animals immunized by living cultures were protected by penicillin or sulphonamides. The type or antigenic state of the Group A strain is not stated.

Batches of mice were immunized for 6 weeks with bi-weekly doses of heat-killed organisms ranging from 10^6 to 2×10^9 organisms. They were challenged after 5 days with 10^4 or 10^7 lethal doses of the homologous organisms. Animals immunized with 10^9 organisms per dose showed marked resistance even after challenge with 10^7 lethal doses and in general protection increased with the vaccinating dose.

Animals treated with penicillin or sulphonamide and injected with a single dose of 0·5 ml. of 10^{-5} dilution (= 10,000 lethal doses) of living culture were not protected when challenged 10 days later with the same dose of organisms. There was some protection when animals were treated with the same dose of living organisms and antibiotics once each week for 4 weeks in succession and animals treated weekly with 1 ml. of 10^{-3} dilution (1–2 million) of organisms with penicillin protection showed marked resistance and their sera passively protected other animals against the homologous organism.

Comparison of the 2 methods of vaccination indicates that protection can be obtained by both techniques if a large enough dose of organisms is given and vaccination continues for long enough. Vaccination with living organisms is more efficient than vaccination with a heat-killed preparation.

[See also this *Bulletin,* 1959, v. 34, 150.]

M. Patricia Jevons

BARKER, S. A., KEITH, M. C. & STACEY, M. **Monosaccharide Sequence in Pneumococcus Type XIV Polysaccharide.** [Correspondence.] *Nature.* 1961, Mar. 4, v. 189, 746–7. [12 refs.]

MIGULINA, V. M. **[Employment of the Method of Fluorescent Antibodies for the Diagnosis of Gonococci]** *Vestnik Dermat. i Venerol.* Moscow. 1961, v. 35, No. 1, 54–8. [In Russian.]

The English summary appended to the paper is as follows:—

"For the purpose of differential diagnosis of the gonococcus the author utilized the method of fluorescent antibodies. Hyperimmune rabbit antisera against the gonococcus and staphylococcus were obtained, out of which gamma-globulin protein fractions were isolated. The latter were subject to conjugation with fluorescein-isocyanate after Coons method. The conjugates obtained were successfully used for direct and cross staining of gonococcal and staphylococcal cultures. The degree of brilliance of fluorescence was dependent on the conjugate series, its dilution, as well as on the age of the culture under study."

NORMAN, J. O. & WILLIAMS, R. P. **Purification of a Material from Egg Yolk Dialysate that stimulates Mycobacterial Growth.** *Texas Reports on Biol. & Med.* 1960, v. 18, No. 4, 636–45, 3 figs. [17 refs.]

The authors have previously reported that egg yolk dialysed against water yields a dialysate that promotes the growth of tubercle bacilli in the minimal medium of Proskauer and Beck [this *Bulletin,* 1960, v. 35, 808]. In the present paper, they show that the active ingredient can be concentrated 65 times by continuous extraction into ether and that it can be further purified by chromatography on paper treated with silicic acid by using either isooctane-ethyl ether or *n*-propanol-water as the partition solvent; the chromatography increased the activity a further 4 times and the position of the active component was detected by bio-autography.

The active component was insoluble in water but soluble in fat solvents, *e.g.* ethanol or chloroform. It contained no carbohydrate, phosphate groups or Kjeldahl nitrogen, and showed a single peak absorption at 279 mμ; it was yellowish in visible light and fluoresced a light blue under ultraviolet light; these properties and its Rf value are similar to those of vitamin K_1.

These studies continue, but the authors are working on the hypothesis that the substance is a quinone or naphthoquinone, perhaps related to coenzyme Q or the vitamin K compounds. *S. R. M. Bushby*

SELKON, J. B., SUBBAIAH, T. V., BHATIA, A. L. RADHAKRISHNA, S. & MITCHISON, D. A. **A Comparison of the Sensitivity to *p*-Aminosalicyclic Acid of Tubercle Bacilli from South Indian and British Patients.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 599–611, 2 figs. [11 refs.]

Routine sensitivity determinations on strains of tubercle bacilli isolated from pre-treatment patients in South India suggested that they were in general more resistant to PAS than those from patients in Britain [this *Bulletin,* 1960, v. 35, 134], and in the investigation described in this paper, strains of tubercle bacilli isolated in India and in Britain were examined both in London and Madras by the same methods on Löwenstein-Jensen medium containing PAS in 2-fold decreasing concentrations. The inocula contained about 10^5 viable units and 3 end-points were read, *viz.* the highest concentrations on which 20, 50 and 100 colonies grew.

The investigation consisted of 3 separate investigations each being modified by the results obtained from the previous one, and in all, strains from 147 Indian and 93 British patients were compared. On reading the sensitivities according to the 50- and 100-colony end-points, no difference was found in the sensitivities of the 2 groups, but when read by the 20-colony end-point the Indian strains were found to contain a small proportion (about 0·02%) of resistant organisms not present in the British strains. These resistant bacilli grew as large colonies in the presence of 2·0 μgm. PAS per ml., but when they were subcultured onto medium containing the same concentration of PAS only a limited amount of growth occurred.

The presence of this resistant moiety in the tubercle bacilli populations is considered to be probably unimportant for there is no evidence that treatment with isoniazid + PAS in India is any less efficient than in Britain, and therefore rather than increase the usual reading of the sensitivity test from the 20-colony to the 100-colony end-point so that the presence of these bacilli

will be ignored, in future the inoculum is to be reduced 10-fold. *S. R. M. Bushby*

ŠULA, L., STOTT, H., KUBÍN, M. & KIAER, J. **A Study of Mycobacteria isolated from Cervical Lymph Glands of African Patients in Kenya.** *Bull. World Health Organziation.* Geneva. 1960, v. 23, Nos. 4/5, 613–34, 12 figs. [31 refs.]

During the period March–June 1958, 57 cervical lymph glands were removed from patients of all ages in Nairobi and sent by air to Prague and there examined bacteriologically and histologically. None of the patients had had antituberculous chemotherapy; 50% of the patients were under 10 years of age and 19% were from 10 to 20 years of age. 40 of the patients had been examined radiologically and 20 of them had evidence of active pulmonary disease while 16 had no abnormality.

41 strains of proved tubercle bacilli were isolated by culture guineapig inoculation or both. All the strains were positive for catalase and peroxidase, and showed characteristic cord formation; they were all sensitive to isoniazid, streptomycin, PAS and Conteben [thiacetazone]. All but one of the strains were virulent to guineapigs, and the animals infected, with the one exception, died of an intercurrent infection, so the virulence was not determined.

32 of the strains were eugonic, niacin-positive and so were accepted as human strains. As none of the remaining 9 strains caused death of rabbits within 8 weeks, they were all regarded as non-virulent for these animals, and 5 grew eugonically and were niacin-positive when recovered from the rabbit. In spite of 2 of the dysgonic strains being niacin-negative, they were regarded as human strains because of the low virulence in guineapigs, and thus all the strains were accepted as human strains. Of the 16 specimens from which no proved tubercle bacilli were recovered, 3 showed no histological evidence of tuberculosis and no acid-fast bacilli were isolated. 5 others contained acid-fast bacilli in sections but the guineapigs were negative and the cultures were contaminated or were sterile. 4 more yielded acid-fast bacilli in guineapigs and the primary culture but the bacilli failed to grow in secondary cultures. 2 were positive by guineapig inoculation but negative by culture and 1 of these was negative histologically. 2 of these specimens were inadvertently sent in formol saline.

The failure to isolate any bovine strains is discussed but the authors maintain that the findings are in accordance with the clinical evidence. However, the identity of the bacilli that were not grown or propagated in subculture must remain in doubt.

The histological examination of the glands showed the changes to be similar to those in tuberculous glands from European patients, and 3 of the glands proved not to be tuberculous. *S. R. M. Bushby*

ŠULA, L., SUNDARESAN, T. K. & LANGEROVÁ, M. **Effects of Storage and Transport on the Cultivability of Mycobacteria.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 635–51, 3 figs.

Previous experience had shown that when the specimens of sputum were sent from Africa to Europe for examination tubercle bacilli were often not grown when the acid-fast bacilli were scanty. In order to see whether the transportation of the specimen had affected the viability of the bacilli, suspensions containing 10^{-3}, 10^{-4}, 10^{-5} and 10^{-6} mgm. of H37Rv in saline were sent from Prague to Entebbe, Uganda, and after 11 days they were returned, a total of 14 days having elapsed since they were dispatched. The suspensions were in glass ampoules, 5 of each dilution and they were kept at temperatures that varied from 5°C. to 25°C. The day after they were received back, duplicate cultures were made from each sample and from duplicate suspensions that had been kept in Prague in the refrigerator; 4 different media were used, including Löwenstein-Jensen medium that was in tubes and Petri dishes.

The growth was compared with that of similar cultures made at the time the original suspensions were made, and the results showed that the percentage of viable bacilli had markedly decreased even in the suspension kept at Prague in the refrigerator, although to a somewhat lesser extent—only 1 of the 50 cultures made from the 10^{-5} suspension and 2 from those from the 10^{-6} suspension grew tubercle bacilli.

Duplicate suspensions in plastic containers were also stored at Prague, to check whether the containers were affecting the survival, and in these tubes viability appeared to be slightly better than in the glass ampoules but the difference was probably not significant.

In order to confirm that a similar reduction of viable bacilli occurred with sputa, 24 specimens of smear-positive sputum were similarly sent to Africa and back, with portions of each being retained at Prague at 2°C. 13 of the specimens were damaged, but the results with the 11 satisfactory specimens confirmed the results with H37Rv—there was a 100–10,000-fold reduction in viable bacilli as compared with the numbers of bacilli grown before the specimens were sent away or stored at Prague. *S. R. M. Bushby*

ŠULA, L., SUNDARESAN, T. K. & LANGEROVÁ, M. **Comparison of the Sensitivity of Löwenstein-Jensen Media prepared in Different National Bacteriological Laboratories.** *Bull. World Health Organization.* Geneva. 1960, v. 23, Nos. 4/5, 653–68, 2 figs.

Data from certain tuberculosis projects assisted by WHO have shown that there is considerable variation in the proportion of positive cultures obtained with specimens, irrespective of whether they are positive or negative by microscopy. In order to determine the role played by the media and the glassware at the centres, arrangements were made for Löwenstein-Jensen medium prepared at Budapest, Copenhagen (2 institutes), Tirana, Warsaw and Zagreb to be sent to Prague, where the growths of H37Rv, Duprey (bovine strain), BCG and pus from guineapigs infected with H37Rv and Duprey were compared on each variety. Samples of the Budapest medium (Kotanyi medium) were freeze-dried and at Prague they were reconstituted, inspissated and included in the comparison. As a check on the effects of the glassware, the Prague medium was prepared in Czechoslovakia tubes and Petri dishes and in Jena tubes from Copenhagen. The medium in the Petri dishes was

inspissated at 3 temperatures, *i.e.* 75°C., 85°C. and 95°C.

Standard inocula were used in 10 tubes of each medium and the results showed that the number of viable units for H37Rv ranged from $18{\cdot}2 \times 10^6$ to $4{\cdot}8 \times 10^6$, and for the bovine strains from $11{\cdot}4 \times 10^6$ to $2{\cdot}0 \times 10^6$. There were also big variations with the BCG inocula and with the recovery of tubercle bacilli from the samples of pus. The media not only varied in sensitivity, the Tirana medium giving the highest counts and the Prague medium the lowest, but there were also big differences in the coefficients of variation of the counts from the 10 tubes of the same medium; although the Tirana medium showed the least variation and the Prague medium the highest, the sensitivity of the other media did not always parallel the degree of variation. The character of the growth on the different media varied from well circumscribed elevated colonies to flat, confluent colonies. The glassware also had a quantitative effect, for the Prague medium became more sensitive when tubed in the Danish tubes, and the growth in Petri dishes on the Prague medium and the Budapest freeze-dried medium was not only more prolific but the difference in sensitivity of the 2 media was reduced. The effects of inspissating at different temperatures had little effect on sensitivity but the colonies were smaller on the medium heated at the higher temperature.

In view of these variations the authors conclude that international comparison of cultural results is not possible at present. *S. R. M. Bushby*

ARTMAN, M. & BEKIERKUNST, A. **Studies on *Mycobacterium tuberculosis* H37RV grown *in vivo*.** *Amer. Rev. Respiratory Dis.* 1961, Jan., v. 83, No. 1, 100–106. [10 refs.]

In a preliminary note, *Nature* (1959, v. 184, 458) the authors reported that tubercle bacilli grown *in vivo* were devoid of dehydrogenase activity because of an inhibitor present in the extract. In the present paper they describe the results of experiments using triphenyltetrazolium chloride as an electron acceptor.

Cell-free extracts of disintegrated BCG and H37Rv grown *in vitro* oxidized both lactate and malate in the presence of the tetrazolium, but a similar extract of the H37Rv obtained from the lungs of moribund mice was incapable of doing this and when it was mixed with the extracts of the bacilli grown *in vitro* it suppressed their ability to oxidize these substrates. Extracts of these *in vitro* bacilli depressed slightly or not at all the activity of succinoxidase of homogenates of normal mouse lung, but the extract of the bacilli grown *in vivo* depressed the activity by approximately 50%.

Because cell-free extract of acetone-dried cells of *Mycobacterium phlei* form an excellent indicator system, owing to their high hydrogen transfer system, experiments were made on them. Cell-free extracts and intact cells of *in vitro* BCG and H37Rv showed no activity under the conditions of the test but they increased the dehydrogenase activity of the *Myco. phlei*, whereas extracts and intact cells of the *in vivo* H37Rv almost abolished it. In the final experiments, extracts of tuberculous mouse lungs, but not of lungs infected with *Klebsiella pneumoniae* or normal lungs were shown to behave similarly to the extracts of the *in vivo* bacilli, but the authors conclude that at this stage it is not possible to decide whether the inhibitory factor is derived from the lung and adsorbed onto the tubercle bacilli, or whether it is from the bacilli themselves.

S. R. M. Bushby

FÖLDES, J. **The Isolation and some Properties of the Components of *Mycobacterium tuberculosis*.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 4, 351–61, 1 fig. [27 refs.]

——. **The Nature of the Specific Polysaccharides of Tubercle Bacilli III.** *Ibid.*, 363–72, 5 figs. [43 refs.]

——. **Chemical and Serological Investigations on the Proteins of *Mycobacterium tuberculosis*.** *Ibid.*, 373–82, 4 figs. [33 refs.]

MAGNUSSON, M.; ENGBAEK, H. C.; WEIS BENTZON, M. **Specificity of Mycobacterial Sensitins. I. Studies in Guinea Pigs with Purified "Tuberculin" prepared from Mammalian and Avian Tubercle Bacilli, *Mycobacterium balnei*, and other Acid-Fast Bacilli** [MAGNUSSON]. *Amer. Rev. Respiratory Dis.* 1961, Jan., v. 83, No. 1, 57–68. [46 refs.] **II. Studies in Guinea Pigs with Purified Sensitin prepared from Unclassified Acid-Fast Bacilli** [MAGNUSSON, ENGBAEK & WEIS BENTZON]. *Ibid.*, 69–84. [46 refs.]

I. In the first of these studies, purified sensitins were obtained from cultures in Sauton medium of 4 strains of human tubercle bacilli, BCG, 3 bovine strains, 3 avian strains, *Mycobacterium balnei, Myco. smegmatis* and 3 strains of unclassified mycobacteria from sputa. Guinea-pigs were sensitized to each of the strains by injecting 2 mgm. of the heat-killed bacilli suspended in light paraffin oil, and tested intradermally with 0·1 ml. of 0·02 mgm. per ml. and 0·002 mgm. per ml. of each sensitin.

Practically no differences in specificity, judged by the difference between the homologous and heterologous reactions, were found in the sensitins from the human and BCG strains, but those from the virulent bovine strains were more closely related to each other than to the human sensitins. No differences were found between the avian strains but these were all different from the mammalian and *Myco. balnei* strains. The other 4 sensitins were different from each other and from the other strains.

II. In the second paper the results of similar studies of 37 unclassified strains show that these bacilli can be grouped according to the specificities of their sensitins. The sensitins of the first paper and 8 others which had previously been shown to have different specificities were included in the study and they formed 17 groups, A–R. The 10 photochromogenic strains (*Myco kansasii*) fell into one group (G), 2 Battey strains fell into

group C, these strains differing from the human and bovine tubercle bacilli (A) and the avian tubercle bacillus (B); the well-known strain ATCC 607 was found to be similar to *Myco. smegmatis* (I). The 2 orange-pigmented strains from India and one from Denmark were placed in group D, but a similar strain from Africa behaved differently. The 8 strains from Africa fell into 5 different groups.

In general the grouping by specificity of sensitins correlated well with those based on other bacteriological criteria. [The descriptions of the strains, their behaviour in Sauton media, and the cross-reactions of the sensitins are given in tabular form, which should be consulted by those especially interested in these mycobacteria.] *S. R. M. Bushby*

BOUVIER, C. A. & BÖHME, D. **Effects of Killed Tubercle Bacilli (BCG) and Constituents upon the Reticuloendothelial System, the Internal Organs, and the Distribution of Circulating Leukocytes of Normal Albino Mice.** *Amer. Rev. Respiratory Dis.* 1961, Jan., v. 83, No. 1, 85–95, 8 figs. [29 refs.]

Groups of mice were injected intraperitoneally with BCG washed thrice with cold acetone, a methanol extract of BCG extracted with acetone at 37°C., the methanol residue after extraction at *p*H 10 with N NaOH, and the extract of the alkali-methanol residue after extraction with N HCl at *p*H 4·0. With each antigen the vaccinating dose was 200 μgm. At various intervals after vaccination mice were killed and examined histologically, and after others had had blood taken from them for differential leucocyte counts, they were injected intravenously with India ink and the rate of clearance of the carbon was determined by estimating electrophotometrically the concentration of the carbon in the blood at intervals. The clearance value of the carbon was expressed as the slope of the curve from plotting the log of the carbon concentration against the time of bleeding, and the phagocytic index was calculated from this slope and the weight of the liver and spleen in relation to the total bodyweight of the animals.

Previous studies have shown that all these antigens afford protection against challenge with organisms unrelated to the tubercle bacillus [this *Bulletin,* 1958, v. 33, 270, 807], and in this present study they all stimulated the ability of mice to clear the blood stream of the carbon. All the antigens also induced the production of epithelioid granulomas without caseation at the site of injection and in the liver, spleen and lymph nodes. Heterotopic haemotopoiesis was frequently encountered, which might have indicated bone-marrow dysfunction. The only evidence of cell multiplication was with the cells involved in the formation of tuberculous structures and there was nothing to indicate that these cells, especially the epithelioid cells, took part in the clearance of the carbon. Only the BCG-acetone extract affected the numbers of circulating leucocytes, and this antigen caused a moderate increase of segmented neutrophils on the 1st–4th days and of the monocytes on the 8th day. *S. R. M. Bushby*

BAUER, J. A., Jr. & STONE, S. H., with the technical assistance of R. I. MCCLESKEY & J. H. GOODE. **Isologous and Homologous Lymphoid Transplants. I. The Transfer of Tuberculin Hypersensitivity in Inbred Guinea Pigs.** *J. Immunology.* 1961, Feb., v. 86, No. 2, 177–89, 7 figs. [35 refs.]

WEIMER, H. E., BELL, R. T., FROMAN, S., NISHIHARA, H. & RICE, E. H. **Electrophoretic Studies of Serum Proteins and Glycoproteins during Early Stages of Experimental Tuberculosis.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 300–303, 4 figs.

This study investigates the rate and extent of changes in electrophoretic patterns in the early stages of an experimental infection with tuberculosis. Adult, virgin guineapigs with an average weight of 750 gm. were found to be non-reactors to intradermal injection of 0·1 ml. of a 5% solution of OT, and were then inoculated with *Mycobacterium tuberculosis,* strain B88. Full general and pathological data are given on the condition of the guineapigs at 8, 15, 19, 29 and 50 days. The only significant change in the protein pattern was increase of alpha 1 globulin in the 8-day group; a further increase was noted 15 days after inoculation, and the fraction remained significantly elevated throughout the experiment. Albumin levels were significantly decreased 15 days post-infection and remained so. Significant increases in the gamma globulin concentrations were first observed in the 19-day group, and a further elevation of the fraction was found in the 50-day group. A significant increase in total glycoprotein was observed 8 days post-infection owing to the elevation of the protein-bound carbohydrates of the alpha globulins. Maximal changes in protein-bound carbohydrates had occurred 15 days after infection, alpha and beta globulin fractions accounting for 90% of the total. Gamma globulin was the only serum subfraction in which polysaccharide and protein curves paralleled each other.

It is suggested that the early alterations in electrophoretic patterns represent primarily systemic manifestations of the inflammatory response. *F. H. Young*

XALABARDER, C. **The So-Called Problem of Unclassified Mycobacteria. A Review.** *Amer. Rev. Respiratory Dis.* 1961, Jan., v. 83, No. 1, 1–15, 10 figs. [128 refs.]

The purpose of this paper was to review the early history of the so-called atypical mycobacteria and to show that much of the confusion as to their identity and relationship to the tubercle bacillus stems from the survival of the erroneous and anachronistic theory of monomorphism. [Of the 128 references, 51 are prior to 1930 and 18 to 1900.]

All the properties that are generally accepted as being characteristic of the tubercle bacillus, including acid-fastness, slowness of growth, biochemical reactions (including susceptibility to drugs) and pathogenicity, are shown to be variable—in fact, the only one thing that is

absolutely typical is the great plasticity and adaptability to an extreme variety of environments.

The review shows that mycobacteria constitute a single group of organisms but with gradations of progressive change. The loss of biological properties, which incidently renders the bacilli toxic to the host and thus pathogenic, is a reversible change. The author claims that this change from saprophyte to pathogen has been demonstrated *in vitro* and he therefore maintains that the so-called atypical mycobacteria probably originate from pathogenic organisms. *S. R. M. Bushby*

Rees, R. J. W. & Hart, P. D'A. **Analysis of the Host-Parasite Equilibrium in Chronic Murine Tuberculosis by Total and Viable Bacillary Counts.** *Brit. J. Exper. Path.* 1961, Feb., v. 42, No. 1, 83–8, 1 fig.

Mice with chronic tuberculosis usually remain alive for many weeks with an apparently stable pulmonary disease and a steady viable bacillary population [this *Bulletin,* 1961, v. 36, 76], and it is tempting to suggest that in these animals the bacilli remain viable but do not divide—that there is a static and not a dynamic state of equilibrium.

In order to test this possibility 60 mice were infected with 8×10^6 viable units of H37Rv and 59 days later 4 of the surviving 37 mice were killed and the total numbers of viable and of stainable bacilli were determined. On day 60, the remaining mice were divided into 2 groups, one of which was from then onwards treated with isoniazid and pyrazinamide in the diet. At intervals, up to day 175, mice from each group were killed and viable and total counts made of bacilli in the lungs.

The results showed that in the untreated mice the numbers of stainable bacilli and viable bacilli were very similar and remained steady throughout the period of observation. In the treated mice the number of viable bacilli fell steadily throughout the period of treatment but the number of stainable bacilli remained constant until about the 21st day of treatment after which it began to fall. The counts from the untreated animals therefore show that unless dead bacilli were removed from the lungs or had lost their acid-fastness, the bacillary population was viable and not multiplying, and as the counts from the treated animals show that dead bacilli are not rapidly removed from the body and that they remain acid-fast, the authors conclude that in this disease the bacilli are in a resting phase rather than in a dynamic equilibrium between multiplication and destruction. *S. R. M. Bushby*

Sachse, H. H. & Neubert, R. Erfahrungen mit einer Modifikation des Tinsdale-Mediums zur Züchtung von Corynebacterium diphtheriae aus Patientenmaterial. [**Experiences with a Modified Tinsdale Medium for the Isolation of *Corynebacterium diphtheriae***] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 3, 343–9. [17 refs.]

In view of the much diminished incidence of diphtheria and the limited experience of many observers at the present day with regard to the appearance of cultures, the authors have considered it desirable to use a second medium in diagnostic work. Clauberg II has been the medium normally in use in their laboratory and they have explored the value of using Billing's modification of the Tinsdale medium (described by Moore and Parsons [this *Bulletin,* 1958, v. 33, 788]) for the control of observations.

Large comparative series have been put up on both media with the general result that in direct plating the Tinsdale medium missed a few which were recognized on the Clauberg medium and that both missed a considerable number which were revealed by plating after preliminary incubation in a fluid enrichment medium. Clauberg II without agar will serve for this purpose.

Overall, the conclusion reached was that the results with Tinsdale were very nearly equivalent to those with Clauberg and diphtheria colonies were more easily detected on account of the yellow-brown halo which develops around them on this medium and is highly specific. The success of the medium seems to depend a good deal on the peptone used. They were able to replace the Difco proteose peptone recommended, which was in short supply, with Orthana-peptone.

J. W. McLeod

Radola, B. J. **Immunoelectrophoresis of Extracellular Diphtheria Proteins.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 11, 493–8, 7 figs. (6 on pl.). [12 refs.]

The filtrates of cultures of *Corynebacterium diphtheriae* normally referred to as crude toxin are discussed by the author as sources of extracellular diphtheria proteins, and he demonstrates by observations on immunoelectrophoresis with this antigenic material and diphtheria antitoxin that the numbers of antigens in such preparations may be very large and tend to increase with the amount of antigen submitted to electrophoresis, but decrease markedly with highly purified toxins of the order of 3,000 Lf to the mgm. of protein nitrogen. The persisting line of precipitation, which is described as the D line, can, however, also be resolved to 3 separate lines. 2 *gravis* strains have been compared with the standard PW8 strain in respect of the immunoelectrophoretic patterns which they produce with antisera. There are certain quite definite differences, but it is suggested that these are mainly quantitative, especially in respect of the components of the D fraction.

J. W. McLeod

Radola, B. J. **Immunoelectrophoretic Studies on the Precipitating Antibodies of Therapeutic Diphtheria Antitoxins.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 11, 499–503, 9 figs. (8 on pl.). [14 refs.]

In the second paper [see above] a special study is made by the same methods on variations in antibodies produced at different times. 30 different diphtheria antitoxins are brought under investigation.

The amounts of the crude toxin and of antitoxin used were both maintained at 200 Lf. These studies showed that there was a very considerable diversity in the number of lines of precipitation subsidiary to the main D component produced by different sera. The studies coincide with those already described in the previous paper in giving evidence for the resolution of the D line to 3 separate lines. This was especially brought out by immunoelectrophoresis of the products of proteolysis of the more highly purified toxin preparations. It is suggested that the variations in the antibody content of the sera which have been demonstrated are due not to variations in the mixtures of antigens demonstrated in the crude toxins but rather to variations in the antigenicity of these substances. Until more is known of the significance of the secondary antigens in the development of pathogenic action by the *Corynebacterium diphtheriae* it is not possible to assess the value of antisera containing different proportions of antibodies subsidiary to that appropriate to essential diphtheria toxin responsible for the D line. *J. W. McLeod*

KONDO, H., KONDO, S. & KUROKAWA, M. **Biological Studies on Diphtheria Toxin. I. The Relation between DLM and DRM.** *Japanese J. Med. Sci. & Biol.* 1960, June, v. 13, No. 3, 91–9. [21 refs.]

JENSEN (*Acta Path et. Microb. Scandinavica*, 1933, Supp. 14) has claimed that the ratio of DRM [MRD] to DLM [MLD] of diphtheria toxin is constant and that MLD/MRD has a value in the vicinity of 3,000. [MRD is the median minimal reacting dose.]

A corollary of this conclusion obviously is that on measuring the minimal skin reacting dose of a toxin one can estimate its minimum lethal dose.

The authors investigated the accuracy of this finding. They point out that this relationship is not, in fact, constant in that where toxin is fractionated by precipitation at lower concentrations of $(NH_4)_2SO_4$ the ratio of MRD to MLD is much higher in the fractions so obtained than in the parent toxin.

Further it was shown that in the process of inactivation by formaldehyde etc., the skin reacting effect of the toxin decreases more rapidly than its lethal effect. *J. W. McLeod*

OEHRING, H. Toxizitätsänderung von *in vitro* gegen Streptomycin resistent gemachten Stämmen des *Corynebacterium diphtheriae*. **[Changes in Toxigenicity associated with the Development of Streptomycin Resistance in *Corynebacterium diphtheriae in vitro*]** *Arch. f. Hyg. u. Bakt.* 1961, Feb., v. 145, No. 1, 61–9. [27 refs.]

Many independent observers have established that tubercle bacilli which have become resistant to the drugs to which these organisms are susceptible such as isoniazid and streptomycin have at the same time suffered a considerable diminution in pathogenicity to the guinea-pig. In view of these facts the effect on toxin production of acquired streptomycin resistance in strains of *C. diphtheriae* has been investigated. 9 strains, of which 2 came from cases of diphtheria and the remainder from carriers, or subjects with rhinitis or ozaena, were rendered resistant to streptomycin by repeated passage in media containing this antibiotic. This group of strains included 2 *gravis* and 7 *mitis* forms.

The original sensitive and derived resistant strains were then compared in respect of their ability to produce lesions in the guineapig and rabbit skin and also by *in vitro* tests for toxin production by Ouchterlony's method. The rather surprising result was that 5 of these strains showed no change in toxin production while in 4 there was a distinct increase. It was also observed that the increase in virulence in the *mitis* strains was associated with increasing roughness of the colony form, and a titratable increase in the amount of acid produced in starch, *i.e.* there was a suggestion of a transformation to the *gravis* form. *J. W. McLeod*

TASMAN, A., VAN RAMSHORST, J. D. & SMITH, L. **Determination of Diphtheria and Tetanus Antitoxin with the aid of Haemagglutination.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 4, 413–29, 4 figs. [11 refs.]

A careful investigation of the relative values of titrations of tetanus and diphtheria antitoxins by the well established methods—skin reactions in the rabbits for diphtheria and toxicity in the mice for tetanus—has been made with techniques in which the agglutination of toxoid-coated red blood corpuscles by antitoxin is investigated directly, or indirectly by determining the amount of toxoid which is required to neutralize antitoxin and prevent such agglutination. Technical descriptions of the methods are given in great detail and the general conclusion is reached that they give results which are very similar to those obtained with the standard methods. *J. W. McLeod*

RELYVELD, E. H., VAN TRIET, A. J., & RAYNAUD, M., with the technical collaboration of O. BEPOLDIN & W. J. VAN RHEE. Étude immologique de sérums de mouton anti-diphthériques. II. Étude sur les anticorps neutralisants et non précipitants. **[Immunological Study of Sheep Anti-Diphtheritic Serum. II. Study of Neutralizing and Non-Precipitating Antibodies]** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 4, 349–79, 18 figs. [26 refs.]

The authors have followed up work already published [this *Bulletin*, 1960, v. 35, 921], in which the thesis is developed that diphtheria toxin is a complex antigen giving rise to more than one antibody. It has been observed that when hyperimmune sheep antidiphtheria sera are prepared the Lr value often markedly exceeds the Lf value. If toxin is added to such sera in the smallest amount which will give rise to precipitation it is then found that the supernatant, although still rich in neutralizing antibody, is devoid of precipitating antibody. Such antibody, although it gives no precipitate

with diphtheria toxin, tends to be carried down as a co-precipitate in the presence of toxin and precipitating antibody.

In gel diffusion tests performed with artificial mixtures of sera containing only neutralizing antibody and one containing precipitating antibody, a zone of visible precipitation occurs as the mixture diffuses towards a reservoir of toxin, whereas the serum containing neutralizing antibody only, gives no such zone. If, however, the neutralizing antibody is marked with radioactive iodine and a photograph of the diffusion plate is produced showing the distribution of radioactivity, a line is obtained between the toxin and the mixed serum reservoirs which corresponds in position to that produced by visible precipitate.

When these antiserum-toxin neutralization curves are prepared with mixtures of toxin and such neutralizing antiserum, a straight line is obtained. It is claimed that the familiar type of humped curve obtained in such observations is due to the modifying effect of the neutralizing antibody on the precipitating antibody. The average horse antiserum contains the 2 forms of antibody in such proportions that the more usual type of precipitation curve is produced.

The neutralizing and precipitating antibodies cannot be separated by differences in electrophoretic mobility.

J. W. McLeod

TURNER, G. C. **Cultivation of *Bordetella pertussis* on Agar Media.** *J. Path. & Bact.* 1961, Jan., v. 81, No. 1, 15–23, 2 figs. on 2 pls. [22 refs.]

"Meat-extract media are suitable for the isolation of *Bordetella pertussis* provided that peptone, which contributes inhibitory factors, is omitted.

"Nicholson and Turner's meat-extract medium [this *Bulletin*, 1955, v. 30, 71] for the isolation of *Bord. pertussis* and *Bord. parapertussis* can be improved by the use of a quarter-strength horsemeat-extract which is 'dephosphated' by heating at *p*H 8·6 and reinforced with 0·25 per cent. L-glutamic acid.

"Blood can be replaced in this medium by 0·2 per cent. charcoal without affecting the viable count from small inocula, although individual colonies are much smaller. Some increase in colony size is achieved by the addition of 0·01 per cent. haematin, but even so the colonies remain smaller on the charcoal medium than on the corresponding blood medium."

BILLAUDELLE, H. **Observations on the Stability of Biologically Active Substances in *Bordetella pertussis*.** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Oct., v. 120, No. 3, 173–85, 1 fig. [29 refs.]

The author has studied the effect of storage in merthiolate [thiomersal] at both *p*H 7·3 and *p*H 8·6 on the immunogenicity and toxicity of a suspension of *Bordetella pertussis* organisms grown in Cohen-Wheeler liquid medium. Studies have also been made of the stability on storage of soluble material and sediment after disintegration of the organisms. It was found that:—

(a) The cell suspensions stored at *p*H 7·3 lost the lethal toxicity for mice but the dermonecrotic toxicity in rabbits remained. The immunogenicity at this *p*H however was quite stable.

(b) Cell suspensions stored at *p*H 8·6 lost both the lethal and dermonecrotic toxicity and although the immunogenicity was not as stable as at *p*H 7·3 much of it remained.

(c) Formalin inactivated the toxicity and the immunogenicity of the soluble material and,

(d) The sediment from disintegrated cells was almost free of toxin and the immunogenicity of this fraction was very stable on storage.

F. T. Perkins

EDMUNDS, P. N. **The Growth Requirements of *Haemophilus vaginalis*.** *J. Path. & Bact.* 1960, Oct., v. 80, No. 2, 325–35. [10 refs.]

17 strains of *Haemophilus vaginalis* incapable of aerobic growth in the absence of blood and mostly isolated from cases of puerperal sepsis were used to find out the growth requirements of the species.

The effect on growth of various additions to certain basal media are described.

To basal peptone agar additions were made of 10% Seitz-filtered human serum, 1% Lab-Lemco, 5% pancreatic digest of horse flesh ("digest") and 5% yeast extract in various qualitative combinations. No growth was found in the absence of serum and optimum growth was obtained when both serum and Lab-Lemco were present. Yeast extract had an inhibitory effect. The efficiency of serum varies from batch to batch and is always a poor substitute for blood.

With a basal digest agar the effect of various additions on growth was observed:—

(1) *Blood*: human blood gave greatest colony size and most pronounced haemolysis.

(2) *Human Serum and Plasma*: [the author seems to use "recalcified citrated plasma" as serum]. Unfiltered serum and plasma gave colonies of good size. Filtered serum added in 5% amounts to digest broth failed to support growth of certain strains.

(3) *Washed Human Red Cells*: 6% additions were as effective as whole blood but haemoglobin, haeme and haemin failed to support growth.

(4) *Washed Human Red Cell Stromata*: 2% additions containing no haemoglobin supported growth.

(5) *Alone or in combination*—1 in 100,000 dilutions of cholesterol, cephalin, and lecithin and 1 in 5,000 nucleic acids were added but gave no aerobic growth. Addition of factor X to cholesterol was without effect. Anaerobically, poor growth on digest agar was improved by any one addition but not appreciably more by all 4 together.

(6) *V and X Factors*: these failed to support growth.

(7) *Catalase*: added to serum digest agar, catalase failed to stimulate growth of *H. vaginalis* although *H. influenzae* and *H. canis* grew on serum digest agar when catalase was present but not in its absence.

Additional experiments showed that growth was scant to heavy in plain thioglycollate broth and poor in Oxoid thioglycollate-resazurin broth. The addition of 5% human plasma yielded good growth in both sorts of media however.

The essential metabolites provided by blood agar diffused readily through Cellophane and permitted

growth on its surface. When a layer of ordinary agar was poured on the surface of the Cellophane before inoculation no growth appeared, owing to the poor diffusion of the nutrients. *Stewart Fletcher*

RITZERFELD, W. & KÜMMEL, J. Untersuchungen zur bakteriologischen Diagnostik von "Haemophilus vaginalis". [**Investigations on the Bacteriological Diagnosis of *Haemophilus vaginalis***] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 3, 334–42, 5 figs. (4 coloured on pl.). [13 refs.]

The results of the investigation of 500 women for the presence of *Haemophilus vaginalis* in their vaginal secretions are recorded. At least 20% yielded cultures of this micro-organism and its possible responsibility for vulvo-vaginitis is considered.

The paper makes a useful contribution to our knowledge of one of the less studied bacteria of the *Haemophilus* group. It appears to be more exacting in its nutritive requirements, more delicate in its growth and more difficult to maintain in subculture than other species of this genus.

Growth was initiated on a 20% sheep blood agar with Difco No. 3 Proteose peptone, NaCl, Na_2HPO_4, and a trace of dextrose, 10 units penicillin per ml. being added to restrain bacteria which may overgrow *H. vaginalis*; and incubation being in an atmosphere with increased CO_2 content.

The sugar fermentations which are limited and rather inconstant are discussed but other metabolic activities are not considered, *e.g.* indole formation. It does not grow well on boiled blood agar but 0·2% haemin could be substituted for blood with good results. The increased growth in the vicinity of colonies of *Staphylococcus aureus* characteristic of other species of *Haemophilus* was not marked. *J. W. McLeod*

MEITERT, T. & MEITERT, Eugenia. Contribution à l'étude de la structure antigénique des *B. pyocyaniques* (*Pseudomonas aeruginosa*). I. Emploi des réactions d'agglutination pour l'étude de 181 souches. [**The Antigenic Structure of *Pseudomonas pyocyanea*. I. The Agglutination Reaction for the Study of 181 Strains**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Dec., v. 19, No. 4, 623–34, 10 graphs. [14 refs.]

STRASDINE, G. A., CAMPBELL, J. J. R., HOGENKAMP, H. P. C. & CAMPBELL, J. N. **Substrate-Dependent Phosphorylation in Resting Cells of *Pseudomonas aeruginosa*.** *Canadian J. Microbiol.* Ottawa. 1961, Feb., v. 7, No. 1, 91–7, 2 figs. [13 refs.]

STEWART, D. J. **A Triple Sugar-Urea-Iron Medium for the Confirmation of *Salmonella* and the Exclusion of *Proteus* Strains.** *J. Applied Bact.* 1960, Apr., v. 23, No. 1, 7–9.

The medium described in this paper is a modification of the ducitol-lactose-iron medium of TAYLOR and SILLIKER [this *Bulletin*, 1959, v. 34, 1281] in which the additional sugar, sucrose, is included to assist in the detection of slow lactose fermenters; many of such organisms are found to ferment sucrose much more rapidly. This is a doubled layer solid medium with the upper layer, containing the 3 carbohydrates and the iron salt, providing the sloped surface and one butt with the lower layer, containing the urea and thiosulphate, providing the main butt. Reference should be made to the original paper for details of preparation of this medium (TSUI medium). [Another modification of Taylor and Silliker's medium has been reported by PAPADAKIS (*ibid.*, 1961, v. 36, 395) and there are probably others also, but only extended observations on these types of media can demonstrate their superiority over the possibly longer methods with less complicated media.] *H. J. Bensted*

i. HARVEY, R. W. S. & PRICE, T. H. **An Economical and Rapid Method for H Antigen Phase Change in the *Salmonella* Group.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service* (*directed by Med. Res. Council*). 1961, Jan., v. 20, 11–13, 1 fig. [11 refs.]

ii. JAMESON, J. E. **A Simple Method for inducing Motility and Phase Change in Salmonella.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service* (*directed by Med. Res. Council*). 1961, Jan., v. 20, 14–16, 1 fig.

Both of these papers describe modifications of the orthodox method of including phase change of the H-antigen complex of diphasic salmonellae. The fundamental principles governing any method of demonstrating the diphasic characters of a salmonella organism, when simple plating technique fails to reveal the two types of colonies, depend on the culture of the organism in a medium which encourages motility and the development of the flagellar antigens and which contains a sufficient concentration of an antiserum, specific for the H antigens already recognized, to suppress or immobilize that phase and allow the second phase to come through, if it is present. There are many methods by which this may be achieved, but they are all modifications of this principle.

i. Harvey and Price employ a Pasteur pipette in which the test culture is in the distal tip of the capillary and the rest of the capillary and shaft of the pipette contain semisolid agar and the antiserum which is intended to suppress the unwanted phase of the salmonella organism under test. The second phase, if present, is collected from the top of the medium in the pipette shaft.

ii. The second paper by Jameson makes use of the fact that filter paper moistened with a culture medium can then act as a sloped culture medium itself. If strips of filter paper so treated are inoculated at one end with certain coliform organisms growth will creep along the strip, under optimum conditions, at a rate which bears some relation to the motility of the organism: a highly motile typhoid bacillus will grow along the strip more quickly than a less motile *Escherichia coli*. By using strips of filter paper previously soaked in the appropriate antiserum the author found that when a diphasic

salmonella organism was inoculated onto one end of such a strip the serum immobilized its own phase and he was able to recover the second phase at the other end of the strip. In its practical application the serum-treated slips were laid in parallel on the surface of a suitable culture medium in a Petri dish and the inoculation onto one end of the strip also included a small area of the adjacent culture medium. After 8–16 hours' incubation at 37°C. preliminary slide agglutination tests may be made by scraping off growth from the opposite end of the strip or the end may be cut off for transfer to broth for more complete serological examination.

For full details of either method the original papers should be consulted. In the hands of the respective authors both methods have given reliable results and appear to be sufficiently simple for application to routine work. *H. J. Bensted*

TAYLOR, Joan, LEE, Margaret M., EDWARDS, P. R. & RAMSEY, Carolyn H. **A New Type of Flagellar Variation associated with New Antigens in the *Salmonella* Group.** *J. General Microbiol.* 1960, Dec., v. 23, No. 3, 583–8.

Phase variation of the flagellar antigens of diphasic salmonella organisms is usually represented: phase 1 $\rightleftarrows$ phase 2 and indicates that the phase change in either direction may be readily induced by simple laboratory techniques. The present paper is concerned with a new type of phase variation which changes in one direction only.

3 new salmonella serotypes, isolated from animal feeding-stuffs or fertilizers, all belonging to O-group E4 showed this type of variation. The O and phase 1 flagellar antigens were common to each: 1,3,19:g,s,t, but the phase 2 antigens, hitherto undescribed, were found to be distinct and were labelled z43, z45, z46 respectively.

In each case natural cultures yielded colonies in either phase 1 or phase 2, but whereas phase 2 colonies could readily be transformed to phase 1, by passage through semi-solid medium containing phase 2 antiserum, no such change could be induced by passaging phase 1 colonies through medium containing phase 1 antiserum; the culture was immobilized.

These observations, in addition to their extreme interest, are of considerable technical importance to specialists studying this complicated group of organisms and also could be important in certain epidemiological investigations. If, for instance, in an original plate culture a single colony isolation is found to have the antigenic formula 1,3,19:g,s,t, this may represent a monophasic Salmonella Senftenberg or it may represent an irreversible g,s,t, form of a diphasic salmonella organism of the type described in this paper. So far, this new type of variation appears to be associated only with organisms carrying z43, z45 or z46 as phase 2, but already z43 has been identified in salmonellae outside the O-group E4 and there seems to be little doubt that extended observations will reveal further examples.

H. J. Bensted

COLOBERT, L. & CREACH, O. Structure de la paroi ectoplasmique d'*Eberthella typhi*. Nature et localisation du substrat du lysozyme. [**Structure of the Cell-Wall of *Salmonella typhi*. Nature and Localisation of the Lysozyme Substrate**] *Ann. Inst. Pasteur.* 1960, Nov., v. 99, No. 5, 672–94, 3 figs. [70 refs.]

This is a biochemical study of the isolated cell-wall of *Salmonella typhi* strain 0–901. The digested material was treated with ethylene-diamine-tetracetic acid and two fractions were obtained—one soluble and the other insoluble. The soluble extract comprised the somatic antigens or endotoxin and could be regarded as constituting the outer layer of the cell-wall. The insoluble extract contained a glucidic fraction and a polypeptide fraction, the make-up of which shows it to be a fundamental constituent of the mechanical structure of the cell-wall. These two fractions are bound to a lipid and form a single component which appears to be the only lysozyme substrate and constitutes the inner layer of the cell-wall.

The author considers that his analysis indicates that the lipid fraction of the lysozyme substrate would be closely related in position to the cytoplasmic membrane and that this arrangement would be maintained by the lattice-like supporting structure which is composed of the deep-layer glycopeptide fraction. This fraction, rich in amino-sugars and diamino-pimelic acid, could, in turn, be bound to the lipid of the somatic antigens with which it could be in contact. The non-bound lipid probably occupies a superficial position in the cell-wall close to the endotoxin-bound-lipid. *H. J. Bensted*

READ, K. S. & FERGUSON, W. W. **Control of Vi-Phage Type of *Salmonella typhi* by Polylysogenicity.** *Ann. Inst. Pasteur.* 1961, Jan., v. 100, No. 1, 120–27. [10 refs.]

GABBRIELLI, G. & MORGANTETTI, F. Il problema del controllo dei vaccini antitifici. Nota IV. Studio sperimentale dei valore immunogeno di vaccini antitifici allestiti con metodi diversi. [**The Problem of Control of Anti-Typhoid Vaccines. Note IV. Experimental Study of Anti-Typhoid Vaccines prepared by Various Methods**] *Riv. Istituto Sieroterap. Ital.* 1960, July–Aug., v. 35, No. 4, 498–504. [21 refs.] English summary (9 lines).

Investigating the prophylactic protection of mice with suspensions of *Salmonella typhi* (Ty2) the authors compared 5 preparations in which different agents were used to kill the bacteria. These were formalin, acetone, alcohol, sublimate and heat. 300 million bacteria were given intramuscularly and 10 days later each group of mice was tested with graded doses of live Ty2 suspended in Ringer's solution and administered intraperitoneally. The index of efficacy was calculated by the method of BONET-MAURY *et al.* [this *Bulletin*, 1954, v. 29, 863].

No significant differences in the protective value of the different vaccines was determined.

[For earlier studies, see this *Bulletin*, 1959, v. 34, 1162]. *J. W. McLeod*

AKSOYCAN, N. & AKMAN, M. 1959 seneside Ankara'da dere sularindan, hastalardan tecrit edilen *S. typhi, S. paratyphi B.* suşlari ve bunlar arasindaki epidemiyolojisel munäsebetler. [**The Strains of *Salm. typhi* and *Salm. paratyphi B* isolated from Stream Waters and from Human Salmonellosis Cases in Ankara during the Year of 1959 and the Relationship between the Strains isolated from these Sources**] *Türk Ijiyen ve Tecrübî Biyoloji Dergisi.* Ankara. 1960, v. 20, No. 3, 419–34. English summary.

3 small streams pass through the city of Ankara, and they are open to heavy contamination. The authors report on 98 strains of *Salmonella typhi* and 42 of *Salm. paratyphi B* isolated from man, and 52 of *Salm. typhi* and 325 of *Salm. paratyphi B* isolated from these streams; these were examined (some by Dr. Nicolle of Paris) for phage types, and the types from man and from the water were closely related (details are given in the Turkish text tables). The streams, therefore, are held to be important in transmission, but are difficult to control.

No *Salm. paratyphi A* were found.

Charles Wilcocks

NESTORESCU, N., POPOVICI, Marcella, TUPA, Sanda & SZEGLI, Lucia. Beitrag zur Lysotypie von *S. paratyphi B* nach Felix und Callow sowie dem "natürlichen System" von Scholtens. [**Contribution to Phage typing of *Salm. paratyphi B* according to Felix and Callow as well as to the "Natural System" of Scholtens**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 2, 216–19. [18 refs.]

The English summary appended to the paper is as follows:—

"If the standard method of FELIX and CALLOW is used exclusively, the determination of the lysotype Dundee may be incorrect.

"The system of 'natural' phages according to Scholtens permits the subdivision of some types of the Felix-Callow-system."

POLANETZKI, U. & BRANDIS, H. Über das Ornithinspaltungsvermögen der Paratyphus-B-Lysotypen. [**On the Ornithine Decarboxylation Capacity of Paratyphoid B Lysotypes**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 2, 220–23.

The English summary appended to the paper is as follows:—

"On the basis of the investigation of 600 strains of S. paratyphi B, belonging to all known phage types it could be demonstrated, that the incapacity to decarboxylate Ornithine can be observed only rarely in approximately 1% of the strains. This biochemical test therefore offers no special advantage for the complementation of phage-typing of S. paratyphi B."

KIESEWALTER, J., RUDAT, K. D. & SEIDEL, G. Salmonellen aus Reptilien. I. Mitteilung: Untersuchungen an Schildkröten. [***Salmonella* Strains isolated from Reptiles. I. Examination of Tortoises**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 503–9. [14 refs.]

The authors, examining Greek tortoises have confirmed the findings of BOYCOTT *et al.* [this *Bulletin*, 1953, v. 28, 856] that tortoises harbour numerous salmonellae which can be recovered from the material taken from their cloacae. 36·5% of 528 such tortoises gave positive results from swabs taken. These included 26 different types; several of these are of recognized pathogenicity for man.

The obvious significance of this is emphasized since it indicates these reptiles as possible sources of infection for man.

J. W. McLeod

DAWSON, G. W. P. & SMITH-KEARY, P. F. **Analysis of the *su-leu* A Locus in *Salmonella typhimurium*.** *Heredity.* 1960, Dec., v. 15, Pt. 4, 339–50.

LE MINOR, L., FERREIRA DE ABREU, E., CHARIE-MARSANES, C. & VALADAO, F. G. Un nouveau sérotype de *Salmonella*, S. manica 1,9,12:*gmst*:z_{42}. [**A New *Salmonella* Serotype, Salm. manica, 1,9, 12:*gmst*:z_{42}**] *Bull. Soc. Path. Exot.* 1960, Sept.–Oct., v. 53, No. 5, 830.

LE MINOR, L., VASSILIADIS, P., VAN ROS, G. & HERMAN, F., with the technical collaboration of C. CHARIE-MARSAINES. Un nouveau sérotype de *Salmonella* S. ruzizi (3,10:*lv*:*enz*$_{15}$). [**A New *Salmonella* Serotype, Salm. Ruzizi (3,10:*lv*:*enz*$_{15}$**] *Bull. Soc. Path. Exot.* 1960, Sept.–Oct., v. 53, No. 5, 776–7.

LE MINOR, L., PINHEDE, N., KERREST, J., ARMENGAUD, M., BAYLET, R. & DREAN, D. Un nouveau sérotype de *Salmonella* S. tilène (1,40:eh:1,2). [**A New *Salmonella* Serotype, Salm. Tilène (1,40:eh: 1,2).** *Bull. Soc. Path. Exot.* 1960, Sept.–Oct., v. 53, No. 5, 777–8.

MÖBIUS, L. & TAUCHNITZ, C. Über eine im Bezirk Leipzig neu aufgetretene *Salmonella*-Species 4,12: z_{10}:e,n,x. [**A New Salmonella, 4,12:z_{01}:*e,n,x* from the Leipzig Area**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 2, 281–2.

GULASEKHARAM, J., VELAUDAPILLAI, T. & SABANATHAN, S. **Three New *Salmonella* Types from Ceylon: S. Kotte, S. Welikade, and S. Lanka.** *Indian J. Med. Res.* 1961, Jan., v. 49, No. 1, 1–2.

YURACK, J. A., LAIDLEY, Rhoda M., FINLAYSON, Margaret & FERGUSON, Mary. **A New *Salmonella* Serotype: S. Canada (4,12;b–1,6).** *Canadian J. Pub. Health.* 1961, Feb., v. 52, No. 2, 72–7.

SEN, R. **Purine requiring Strains of Shigellae.** *J. Bacteriology.* 1960, Nov., v. 80, No. 5, 585–9, 1 fig. [20 refs.]

During his studies on the nutritional requirements of the members of the *Shigella* group this author has previously drawn attention to a strain of *Sh. dysenteriae* I (Shiga's bacillus) which he found to be cystine-dependent [this *Bulletin*, 1960, v. 35, 926] and now among the mannite-fermenting shigellae he reports 2 strains, *Sh. boydii* 3 (NCTC 9329) and *Sh. boydii* 6 (NCTC 9771), which are purine-dependent. With both strains the growth response with adenine was better than with any of the other purines tested. With strain 9329 growth was better with adenine alone than with combinations of adenine, guanine and uracil, but with strain 9771, although adenine alone gave the best results, the combination of adenine, guanine and uracil gave better growth than adenine and guanine without uracil.

H. J. Bensted

TALAYEVA, J. G. **Survival of Dysentery Bacteria in Water according to the Results of a Reaction with Haptenes.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 3, 314–20.

This paper reports the time survival of Flexner and Sonne bacilli in water from various sources experimentally infected with these organisms under artificial conditions. The results of normal bacteriological methods for the detection of these bacteria are compared with the so-called haptene reaction of RAVICZ-BIRGER. The technique of the haptene reaction is very inadequately described but it would appear that acid extracts of young field cultures of infected waters contain specific precipitinogens which react with high-titre dysentery precipitating sera. It is claimed that the haptene reaction continues to be positive for a much longer period than the period over which the specific organism can be isolated by normal cultural techniques. For instance Flexner bacilli may continue to be isolated from an infected water for up to 9 days, but the same water may continue to be infective, as shown by this haptene reaction, for a further 12 days. *H. J. Bensted*

MATSUMURA, T. & MATSUSHIMA, S. **On Cross Allergic Reaction by *Escherichia coli* and *Shigella* having Common O-Antigen.** *Gunma J. Med. Sci.* Maebashi. 1960, Sept., v. 9, No. 3, 171–3.

"In guinea pigs sensitized with *Escherichia coli* 0–13, antigen of *Shigella flexneri* 2b induced the Arthus phenomenon, systemic anaphylactic shock, and the Schultz-Dale reaction, as did the homologous antigen. The O antigen is partly common to both of these strains. With *Sh. sonnei* antigen, which does not have O antigen in common, these reactions did not occur. Similarly, no reactions were produced with *E. coli* and *Sh. flexneri* antigens in non-sensitized animals. It is concluded that the cross allergic reactions were produced by the O antigen common to *E. coli* and *Sh. flexneri*."

QUESNEL, L. B. **The Behaviour of Individual Organisms in the Lag Phase and the Formation of Small Populations of *Escherichia coli*.** *J. Applied Bact.* 1960, Apr., v. 23, No. 1, 99–105, 5 figs. [17 refs.]

The lag phase of *Escherichia coli* has been studied by direct observation for 4 generations by growing the organisms under the microscope in the improved continuous culture chamber described by POWELL (*J. Roy. Microscopical Soc.*, 1956, v. 75, 235). Essentially the chamber consists of a stretched Cellophane membrane under which a chemically defined culture medium is circulated at a slight positive pressure. Diluted overnight cultures were inoculated on to the upper surface of the membrane, covered with a No. 1 cover-slip. Observations were made at a magnification of × 1500 with transmitted phase contrast illumination.

With increasing age of population the generation time decreased; in most cases the 1st division times were long compared with the subsequent generation times. The author's observations suggest that the lag phase normally seen in stationary cultures is due to, and affected by, 4 factors: (i) a period, with a minimum of about 30 minutes, in which no cell division occurs, (ii) a further period of up to 3 hours before all the organisms not falling into the group with the shortest 1st division times will have divided, (iii) the presence of relatively large numbers of non-viable organisms as compared with such numbers in lag phase, and (iv) prolongation of generation times extending into the 3rd and 4th and possibly into the 5th generation. *H. J. Bensted*

TAYLOR, Joan, WILKINS, M. Patricia & PAYNE, J. M. **Relation of Rabbit Gut Reaction to Enteropathogenic *Escherichia coli*.** *Brit. J. Exper. Path.* 1961, Feb., v. 42, No. 1, 43–52. [17 refs.]

The ligated rabbit-gut test was introduced by DE and CHATTERJE [*Trop. Dis. Bull.*, 1954, v. 51, 581] as a possible test for the pathogenicity of cholera vibrios and considerable interest was aroused when the results were published. Further investigation of the test clearly showed that there was no satisfying explanation for this gut reaction and when the experiments were translated to the "enteropathogenic *Escherichia coli*" the results were not as straightforward as might have been hoped. Apart from the difficulty of assessing a biological response which could be recognized by increased exudate and dilatation of the gut wall the results with strains assumed to be pathogenic were rather irregular. The early experiments of Dr. Taylor and her colleagues [this *Bulletin*, 1959, v. 34, 481] demonstrated that a particular strain of *E. coli* O 26, isolated from a moderately severe case of infant diarrhoea, regularly produced a positive loop-reaction whereas a strain of *E. coli* O 111, isolated from the stool of a healthy baby, always failed to cause any dilatation or inflammatory reaction of the ligated rabbit gut. In the present paper the authors have extended their observations to include a large number of strains of various serotypes of *E. coli* isolated from different sources and also examined a number of factors which might influence the reaction, such as conditions of growth, S–R variation, etc.

The most important findings were that strains of *E. coli* causing, or considered to have caused, infant gastro-enteritis gave a positive rabbit-gut reaction whereas strains isolated from human urinary infections and other sources, where the organism might be assumed to be pathogenic, generally gave negative reactions. The authors conclude from this that the ability of *E. coli* to cause dilatation and inflammation of the rabbit gut is restricted to those strains which cause infant diarrhoea so that the test is one for enteropathogenicity rather than for general pathogenicity. The reaction would appear to be controllable when the inoculated culture is mixed with strain-specific antiserum but it is a little uncertain how far this is related to a particular strain-specificity or to a serotype-specificity. While there is a good deal of evidence to indicate strain-differences within one serotype of enteropathogenicity, as assessed on clinical observations, there is often considerable variation in the response of infants to infection with presumably the same strain, which is due largely to a number of uncontrollable factors. [It is not clear how valuable the rabbit-gut test is likely to be in such a series of controlled experiments because the factor responsible for the gut reaction is still unknown. An illustration of the complicated problems involved is shown by the wide differences in the virulence to chick embryos of strains of the same serotype of *E. coli* belonging to the so-called enteropathogenic group. In a recent paper FINKELSTEIN and RANSOM [*Trop. Dis. Bull.*, 1961, v. 58, 196] describe some interesting protective properties of a strain of *E. coli*, O 111, not exhibited by other strains of the same serotype, on an 11-day chick embryo subsequently infected with *Vibrio cholerae*. This strain of *E. coli* O 111 was of very low virulence to chick embryos whereas other strains of O 111 tested were highly virulent. The variation in virulence of different strains of O 111 for the chick embryo was said to be unrelated to their human enteropathogenicity.

This paper is of considerable interest, but there is still much that is not understood about the rabbit gut reaction, and further investigation is desirable.]

H. J. Bensted

STENZEL, W. Untersuchungen über die Harnblasenpathogenität einger Enterobacteriaceen-Gruppen im Bingelschen Versuch. [**Investigations employing Bingel's technique on the Capacity of Various Groups of Enterobacteriaceae to produce Lesions of the Urinary Bladder**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 2, 123–32, 4 figs. [17 refs.]

Bingel has pointed out that dysentery bacteria are capable of producing lesions of the urinary bladder in the guineapig. The author, using the technique of injecting infective cultures with a fine capillary glass pipette to the bladder of female guineapigs, has compared the results obtained with a wide selection of dysentery strains, a number of salmonellae and a collection of coliforms which included *Escherichia*, Paracolon, Providentia, Ballerup-Bethesda, *Aerobacter* and "Dyspepsie Coli" strains. Only the salmonellae produced lesions resembling those caused by the shigellae. Both groups were liable to cause death but the haemorrhagic lesions were more pronounced with the shigella strains and the bacteria did not penetrate the body in the way that the salmonella were liable to do.

There was a close correspondence between the capacity of shigella strains to infect the bladder and to cause conjunctivitis in the guineapig.

[There is no mention of investigations with the proteus and pyocyaneus groups of bacteria which are so important in cystitis in man.] *J. W. McLeod*

JARVIS, F. G., MESENKO, M. T. & TIBBS, K. E. **Production of Vi Antigen on a Chemically Defined Medium by a Coliform Bacterium.** *J. Bacteriology.* 1960, Nov., v. 80, No. 5, 673–6, 2 figs. [19 refs.]

The coliform bacterium referred to in the title of this paper is strain 5396/38 which is variously regarded as an *Escherichia* or a *Citrobacter* (*freundii*) [this *Bulletin*, 1958, v. 33, 507]. The basal ingredients in the defined medium used were: glucose, 7·5 gm.; Na_2HPO_4, 6·0 gm.; KH_2PO_4, 3·0 gm.; $(NH_4)_2SO_4$, 1·25 gm.; and $MgSO_4 \cdot 7H_2O$, 0·3 gm. per litre of medium. The addition of calcium pantothenate was necessary for optimal growth of the organism and sodium glutamate for optimal production of Vi antigen. NaCl up to a concentration of 0·5% increased bacterial cell yields and also Vi antigen production, but beyond this concentration NaCl had an inhibitory effect on the development of Vi antigen. The growth curve (as measured by turbidity) ran parallel with the total antigen production for about 10 hours' incubation with antigen production flattening out above the growth curve. The distribution of Vi antigen, as found in the bacterial cells themselves and already released into the medium during growth is of considerable interest. The 2 curves cross after about 15 hours' incubation when the Vi antigen found in the cells is beginning to fall and that found free in the medium continues to rise steadily. *H. J. Bensted*

JARVIS, F. G., MESENKO, M. T. & KYLE, J. E. **Electrophoretic Purification of the Vi Antigen.** *J. Bacteriology.* 1960, Nov., v. 80, No. 5, 677–82, 2 figs. [20 refs.]

Many investigators have attempted to purify the Vi antigen and the descriptions of the products obtained in terms of their chemical and biological properties vary considerably. While many of the discrepancies may be related to the different degrees of purity of the end product it must not be forgotten that an antigen of the nature of the Vi antigen may not be able to stand up to the chemical treatment exhibited during the process of "purification"; less vigorous methods are probably desirable and the milder electrophoretic procedures indicated in this paper are worthy of consideration. The method of purification of Vi antigen by continuous flow, paper curtain electrophoresis as set out in this paper should be studied in the original. It appears to yield an article of considerable purity and the results reported are of interest. *H. J. Bensted*

CLEMENT, Mary T. **Effects of Freezing, Freeze-Drying, and Storage in the Freeze-Dried and Frozen State on Viability of *Escherichia coli* Cells.** *Canadian J. Microbiol.* Ottawa. 1961, Feb., v. 7, No. 1, 99–106, 2 figs. [17 refs.]

LION, M. B. & BERGMANN, E. D. **The Effect of Oxygen on Freeze-Dried *Escherichia coli*.** *J. General Microbiol.* 1961, Feb., v. 24, No. 2, 191–200, 5 figs. [13 refs.]

MOROWITZ, H. J. & CASTRO, Elisea. **Amino Acid Composition of the Positive, Neutral, and Negative Peptides of Trypsin-Digested *Escherichia coli* Protein.** *Biochim. et Biophys. Acta.* 1961, Jan. 1, v. 46, No. 1, 33–7.

LINZ, R. & LECOCQ, E. Sur la réactivation d'*Escherichia coli* après traitement par les rayons ultra-violets. I. Réactivation en bouillon et à l'obscurité. [**Reactivation of *E. coli* after Treatment by Ultra-Violet Rays**] *Ann. Inst. Pasteur.* 1960, Nov., v. 99, No. 5, 743–56.

The strains of *Escherichia coli* employed in the experiments recorded in this paper were strains B and K12, both of which are sensitive to the action of ultra-violet (UV) light. Tetracycline-resistant variants were also used in some experiments.

Bacterial cells inactivated by irradiation (UV) could be re-activated by transferring them to nutrient broth and incubating them in the dark at 37°C. As compared with non-irradiated control cells the treated cells multiply very slowly and at the end of 20–24 hours' incubation the number of viable cells may be from 3 to 12 times less per ml. than will be found in the control cultures. After further incubation normal cell death begins to affect the steepness of the growth curve of the control cultures, but the irradiated cell growth curve shows no such flattening so that by the end of 48 hours there is little difference in the viable cell counts of the test and control specimens. There is no evidence to show that UV irradiation induces any genetic change in the cells or that any diffusible substance is involved. It would appear that the inhibitory effect of the irradiation is restricted to the local effect on the cells themselves.

Tetracycline-resistant variants of *E. coli* B show increased resistance to tetracycline after irradiation, as compared with controls, and become tetracycline-dependent. This property continues throughout reactivation but is lost when the multiplication of the variant in broth in the late stage masks the reactivation. The tetracycline-resistant variant of *E. coli* K12 does not display this property. *H. J. Bensted*

DRAKULIC, M., STAVRIC, S. & ŠMIT, S. **On the Metabolic Stability of Nucleic Acids in U.V.-Irradiated *Escherichia coli* B.** *Biochim. et Biophys. Acta.* 1961, Feb. 12, v. 47, No. 1, 114–22, 5 figs. [11 refs.]

FOX, G. & BROWN, J. W. **Protein Degradation in *Escherichia coli* in the Logarithmic Phase of Growth.** *Biochim. et Biophys. Acta.* 1961, Jan. 15, v. 46, No. 2, 387–90, 1 fig.

TUVE, T. & WILLIAMS, H. H. **Metabolism of Selenium by *Escherichia coli*: Biosynthesis of Selenomethionine.** *J. Biol. Chem.* 1961, Feb., v. 236, No. 2, 597–601, 5 figs. [25 refs.]

PRIMOSIGH, J., PELZER, H., MAASS, D. & WEIDEL, W. **Chemical Characterization of Mucopeptides released from the *E. coli* B Cell Wall by Enzymic Action.** *Biochim. et Biophys. Acta.* 1961, Jan. 1, v. 46, No. 1, 68–80, 3 figs. [23 refs.]

v. HOFSTEN, B. **Fluoro-D-Galactosides as Substrates and Inducers of the β-Galactosidase of *Escherichia coli*.** *Biochim. et Biophys. Acta.* 1961, Mar. 18, v. 48, No. 1, 159–63, 3 figs. [10 refs.]

——. **The Inhibitory Effect of Galactosides on the Growth of *Escherichia coli*.** *Ibid.*, 164–71, 7 figs.

——. **Acid Phosphatase and the Growth of *Escherichia coli*.** *Ibid.*, 171–81, 9 figs. [22 refs.]

ZAMIR, Ada, BEN-ISHAI, Ruth. **A Requirement for 2-Thiouracil of 2-Thiouracil-Grown *Escherichia coli* under Conditions of Ornithine Transcarbamylase Repression.** [Correspondence.] *Nature.* 1961, Mar. 18, v. 189, 922–3, 2 figs.

GIBSON, F., GIBSON, Margaret I. & YANOFSKY, C. **A Mutational Alteration of the Tryptophan Synthetase of *Escherichia coli*.** *J. General Microbiol.* 1961, Feb., v. 24, No. 2, 301–12, 6 figs. [13 refs.]

HICKS, R. Marian. **The Effect of Isoniazid, Carbutamide, Propamidine and Pentamidine on the Transaminases and Growth of *Escherichia coli*, Strain 15, Mutant M_2.** *Biochim. et Biophys. Acta.* 1961, Jan. 1, v. 46, No. 1, 143–51. [17 refs.]

HICKS, R. Marian. **The Effect of Isoniazid, Carbutamide, Propamidine and Pentamidine on the Activity and Synthesis of β-Galactosidase, and the Synthesis of Transaminases in *Escherichia coli*, Strain 15, Mutant M_2.** *Biochim. et Biophys. Acta.* 1961, Jan. 1, v. 46, No. 1, 152–8, 3 figs. [15 refs.]

FRANZEN, J. S. & BINKLEY, S. B. **Comparison of the Acid-Soluble Nucleotides in *Escherichia coli* at Different Growth Rates.** *J. Biol. Chem.* 1961, Feb., v. 236, No. 2, 515–19, 3 figs. [16 refs.]

CHAKRABORTY, K. P. & HURLBERT, R. B. **Role of Glutamine in the Biosynthesis of Cytidine Nucleotides in *Escherichia coli*.** *Biochim. et Biophys. Acta.* 1961, Mar. 4, v. 47, No. 3, 607–9, 1 fig.

MANDELSTAM, J. **Isolation of Lysozyme-Soluble Mucopeptides from the Cell Walls of *Escherichia coli*.** [Correspondence.] *Nature.* 1961, Mar. 11, v. 189, 855–6, 1 fig. [13 refs.]

ENGELBERG, Hanna & ARTMAN, M. **Studies on Streptomycin Dependent Bacteria: Effect of Growth in Limiting Amounts of Streptomycin on Respiration and Fermentation of a Streptomycin Dependent Mutant of *Escherichia coli*.** *Biochim. et Biophys. Acta.* 1961, Mar. 4, v. 47, No. 3, 553–60, 2 figs. [18 refs.]

BLAKLEY, E. R. & CIFERRI, O. **Oxidation of Gluconate, 2-Deoxy-D-Glucose, and Lactic Acid by an Enzyme Preparation from *Aerobacter aerogenes*.** *Canadian J. Microbiol.* Ottawa. 1961, Feb., v. 7, No. 1, 61–73, 3 figs. [41 refs.]

COETZEE, J. N. & SACKS, T. G. **Transduction of Streptomycin Resistance in *Proteus mirabilis*.** *J. General Microbiol.* 1960, Dec., v. 23, No. 3, 445–55, 1 fig. [31 refs.]

5 of 11 phages grown on strains of *Proteus mirabilis* resistant to streptomycin transduced the factor causing streptomycin resistance to streptomycin-sensitive bacteria of the same strain, and 3 of the phages were capable of transduction to bacteria of other strains. Transduction rates varied from about 1×10^{-6} to 6×10^{-8} per phage particle adsorbed. The newly acquired character was stable in the transduced clones. Most of the clones became lysogenic and therefore insensitive to the phage and unable to adsorb it. The transducing ability of the phages was less sensitive than plaque-forming ability to inactivation by UV irradiation, confirming that the 2 properties are separate. The expression of streptomycin resistance by the transduced bacteria was delayed and did not develop fully until 6 hours after phage and cells were mixed. After transduction, plating with lower concentrations of streptomycin led to the recovery of more streptomycin-resistant colonies at earlier times than plating with higher concentrations of streptomycin. It appears therefore that the complete phenotypic expression of the acquired character happens gradually, perhaps because the new gene cannot exert its influence until the pre-existing material has been exhausted by a number of cell divisions. *Janice Taverne*

DURLAKOWA, Irena. **Studies on the Antigenic Structure of *Klebsiella* Bacilli isolated in Wroclaw.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 4, 631–44. [48 refs.]

DURLAKOWA, Irena, PRZONDO-HESSEK, Anna & MARESZ-BABCZYSZYN, Jadwiga. **O-Antigens of *Klebsiella* Types K:63–K:72.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 4, 645–54. [21 refs.]

BARBER, C., STAMATESCU, S. & WISNER, B. Cercetări asupra antigenelor capsulare si somatice ale Klebsiellelor (B. Friedländer). **[Studies on the Capsular and Somatic Antigens of *Klebsiella* (Friedländer's Bacillus)]** *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1958, v. 9, No. 4, 499–504, 2 figs. on pl. French summary.

OLITZKI, A. L. **The Antigenic Relationship between Phenol Extracted Bacterial Deoxyribonucleic Acid and other Soluble Antigens of Brucellae studied with the aid of the Agar Gel Precipitation Technique.** *Brit. J. Exper. Path.* 1960, Dec., v. 41, No. 6, 623–32, 7 figs. on pl. [10 refs.]

Deoxyribonucleic acid proteins were isolated from brucellae with phenol, followed by further purification, which were antigenically identical to those isolated by BRAUN *et al.* (*Nature*, 1957, v. 180, 1356). They were highly antigenic but it was not possible to differentiate between the DNA-conjugated proteins isolated from *Brucella abortus*, *Br. melitensis* and *Br. suis* by serological methods. The precipitation line common to all 3 antigens was situated close to the serum source in the same zone as band 5 which was produced by bacterial extracts obtained either by mechanical disintegration or by sonic vibrations, but it was not possible to say definitely whether or not the DNA-proteins are identical with antigen 5. There was no evidence to show that any of the DNA-proteins was specific for a single *Brucella* species.

In addition to the precipitins in the DNA-immune sera there were also relatively high titre agglutinins. These appear to have been due to the presence in the preparations of small amounts of antigen derived from the bacterial cell-wall since they were shown to contain diamino-pimelic acid. It was found possible to absorb out the agglutinins with bacteria treated with acetone, leaving intact the precipitins reacting with DNA-conjugated proteins. *H. J. Bensted*

SCHLAMM, N. A. **Detection of Viability in Aged or Injured *Pasteurella tularensis*.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 818–22.

In investigating the aerosol decay rate in the case of *Brucella tularensis* it was found that certain agar culture media were as suitable as a living animal host for the detection of viability, but for the assessment of infectivity of stored aerosols the route of challenge was most important. Reduction of infectivity of aged airborne *Br. tularensis* was detected only when mice were challenged by the respiratory route; the intraperitoneal route was not suitable for this purpose.

H. J. Bensted

ROBINSON, Diana A. & MILLS, R. C. **Oxidation of Reduced Pyridine Nucleotides in *Pasteurella tularensis*. I. Distribution of Diaphorases and Transhydrogenases.** *Biochim. et Biophys. Acta.* 1961, Mar. 18, v. 48, No. 1, 77–84. [25 refs.] **II. Separation of Diaphorases and Transhydrogenases.** *Ibid.*, 85–92, 1 fig. [12 refs.]

EISLER, D. M. & VON METZ, Eleanor. **Precipitins against *Pasteurella pestis* in Normal and Antibacterial Sera.** *J. Immunology.* 1961, Jan., v. 86, No. 1, 17–21. [14 refs.]

"The normal sera of seven animal species, including sera of germ-free mice and of a Caesarian delivered calf, gave precipitin reactions with fraction IB of *Pasteurella pestis* and with antigens of other Gram-negative bacterial species in agar diffusion plates. The normal precipitin lines were intensified, and additional lines due to specific antibodies were demonstrated in tests with the sera of mice and rabbits inoculated with fraction IB. The normal serum precipitins of Namru strain mice were low in titer. The number of lines could be varied by altering both antigen-antibody concentrations and the *p*H of the agar in which tests were made.

"The normal sera of six mammalian species formed a continuous precipitin line when tested with fraction IB in a single agar diffusion plate.

"Precipitins in normal sera and fraction IB antisera were not specific for 'H' or 'O' antigens of *Proteus vulgaris*. Chemical fixation of these antigens in some instances altered their precipitin reaction with some sera.

"An antigen common to *P. pestis* and *Proteus mirabilis* did not elicit protective antibodies against *P. pestis*.

"The precipitins in calf and cow sera were not demonstrable in commercially available bovine plasma fractions. Human globulin gave precipitin reactions with an antigen common to several bacterial species.

"The precipitins in normal sera and fraction IB antisera of mice were associated with β- and γ-globulins."

STAMATIN, N. La génétique de la sporogenèse chez *B. anthracis*. Note I. Existe-t-il des races génétiquement asporogènes? **[The Genetics of Spore Formation in *B. anthracis*. I. Are their any Races Genetically Incapable of Forming Spores?]** *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Dec., v. 19, No. 4, 493–9. [10 refs.] Note II. Le rôle du phage dans la formation des spores chez les souches peu sporogènes. **[The Part played by the Phage in Spore Formation by Weakly Sporogenic Strains]** *Ibid.*, 501–6.

BITTNER, J. & VOINESCO, Viorica. Quelques données expérimentales sur le mécanisme de l'immunité antigangréneuse. **[Experimental Data concerning the Mechanism of Anti-Gangrenous Immunity]** *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Dec., v. 19, No. 4, 601–15, 4 figs. [53 refs.]

GASTINEL, P., VAISMAN, A. & DUNOYER, F. Problèmes de l'incubation locale de *Spirocheta pallida* dans la syphilis du lapin. **[Problems of the Local Incubation of *Treponema pallidum* in Rabbit Syphilis]** *Ann. Inst. Pasteur.* 1961, Jan., v. 100, No. 1, 1–12, 2 figs.

It has long been known that *Treponema pallidum* spreads rapidly all over the body after inoculation and is present in the blood and lymphatic streams within a matter of hours or even minutes; however, local incubation at the site of inoculation is less well understood.

These authors inoculated two strains of virulent spirochaetes into the testicles and skin of rabbits, some fresh and some immune. At various times after inoculation, specimens were taken from the inoculation sites and examined for spirochaetes by means of dark ground, silver impregnation and sections. Within 2 hours the number of spirochaetes diminishes almost to vanishing point but there are seen numerous granules and spiral filaments which may be stages in the life-cycle of the organisms and which take up the silver stain, the former more so than the latter. After about 14 days, normal spirochaetes reappear but short organisms can still be seen. The various methods of examination yielded essentially the same results.

It is of interest to note that in animals previously rendered immune, spirochaetes disappeared in the same way as in fresh animals but did not reappear and the same applied when killed spirochaetes were injected.

[See also this *Bulletin*, 1949, v. 24, 862.]

T. E. Osmond

HALDAR, D., GHOSH, B. K. & CHATTERJEE, A. N. **Observations on the Mode of Action of Antibiotics on *Vibrio cholerae*.** *Ann. Biochem. & Exper. Med.* Calcutta. 1960, July, v. 20, No. 7, 189–94, 2 figs. [35 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 685.]

SEAL, S. C. **Some Preliminary Observations on Soluble Toxin of Cholera Vibrio.** *Ann. Biochem. & Exper. Med.* Calcutta. 1960, Aug., v. 20, No. 8, 205–16, 2 figs. [46 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 684.]

MUKERJEE, S., GUHA ROY, U. K. & RUDRA, B. C. **Studies on typing of Cholera vibrios by Bacteriophage. Part III: Phage Typing of Strains from Calcutta Epidemics of 1959.** *Ann. Biochem. & Exper. Med.* Calcutta. 1960, July, v. 20, No. 7, 181–8, 1 fig. [12 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 684.]

BACTERIOPHAGES

BRADLEY, D. E. & KAY, D. **The Fine Structure of Bacteriophages.** *J. General Microbiol.* 1960, Dec., v. 23, No. 3, 553–63, 12 text figs. & 34 figs. on 4 pls. [10 refs.]

22 different phages have been stained by the "negative contrast" technique of BRENNER *et al.* [*J. Molecular Biol.* London, 1959, v. 1, 281; this *Bulletin*, 1960, v. 35, (399)], with phosphotungstate or phosphomolybdate, and examined under the electron microscope. Broadly they fell into 3 morphological groups: (1) Phages with a contractile tail sheath, *e.g.* typhoid phages 3T+, C4 and 66F. These were indistinguishable from coliphage T2. They possessed a hexagonal head and a tail which was surrounded by a sheath marked with cross-striations and which ended in a base-plate with several prongs. In the same group, typhoid phage 2 had a differently shaped head and a base plate without any prongs. (2) Phages without a contractile tail sheath, *e.g.* coliphages T5 and T1, typhoid phages 1 and S1 BL. Even when the phage DNA had been released (recognized by the fact that the empty head was filled with phosphotungstate) the tail showed no signs of contraction. Some phages in this group had very long tails, *e.g.* staphylococcal phages 6, 3B and 77, and some had shorter tails, *e.g.* staphylococcal phage 187 and *Pseudomonas pyocyanea* phages Pc and Pz. Phage 3 ML of *Streptococcus lactis* had a head without sharp angles and a tail without a sheath and no neck where it joined the head. (3) Phages with a short stumpy tail, *e.g.* coliphage T3 and a phage active on *Brucella abortus*.

In discussion the authors remark on the variety of tail end-plates observed, some ending with prongs, some with a knob and some with a rounded or pointed tip. Relating morphology to function, they point out that it is not known how phages without a contractile tail sheath penetrate the bacterial cell wall.

Janice Taverne

NELSON, E. L. & GOODMAN, R. E. **Adsorption of Bacteriophage by Hemoglobin Particles.** *Virology.* New York. 1961, Feb., v. 13, No. 2, 257–8.

SOLLER, A. **Procedure for Rapid Concentration of Phage Lysate.** *Virology.* New York. 1961, Feb., v. 13, No. 2, 267–8.

HOFFEE, Patricia, WEINBERG, R. & ENGLESBERG, E. **Absence of the Glucose Effect on the Frequency of Lysogenization in *Salmonella typhimurium*.** [Correspondence.] *Nature.* 1961, Jan. 14, v. 189, 160–61. [10 refs.]

ENTNER and ENGLESBERG reported earlier [this *Bulletin*, 1959, v. 34, 682] that infection of *Salmonella typhimurium* LT2 by phage PLT22 in a medium to which glucose had been added resulted not in bacterial lysis but in lysogeny. Lysogenic and lytic responses were then distinguished by the appearance of turbid and less turbid plaques. This paper reports that when the experiments were repeated with a different technique for distinguishing the responses, the addition of glucose was found to have no effect. Here, indicator bacteria were used which did not ferment galactose and mixtures were plated on a medium containing galactose. On this medium, infected cells undergoing lysis formed plaques in 18 hours; lysogenic cells formed dark colonies surrounded by haloes in 48 hours; and uninfected cells formed dark colonies without haloes. The frequency of lysogenization was not increased by adding glucose during or after adsorption of the phage.

Janice Taverne

DELIHAS, N. **The Ability of Irradiated Bacteriophage T2 to initiate the Synthesis of Deoxycytidylate Hydroxymethylase in *Escherichia coli*.** *Virology.* New York. 1961, Feb., v. 13, No. 2, 242–8, 4 figs. [23 refs.]

FÖLDES, J., MERÉTEY, Katalin & VARGA, I. **Isolation and some Properties of the Phages of *B. cereus* NRRL 569.** [Correspondence.] *Nature.* 1961, Jan. 14, v. 189, 161–2, 2 figs.

Phages specific for *Bacillus cereus* 569 were isolated from samples of soil and were found to form plaques of 3 types: clear, target-like and turbid. They did not attack *B. megaterium*, *B. subtilis* or *B. anthracis* and they did not grow in all strains of *B. cereus*. Autolysates of those strains of *B. cereus* which were sensitive to the phages did not precipitate antibody to anthrax polysaccharide.

Thus phage sensitivity could be correlated with cell wall structure. Cell walls of *B. cereus* strains which were not attacked by the phages and which cross-reacted with antibody to anthrax polysaccharide consist of galactose and glucosamine [IVANOVICS and FÖLDES, this *Bulletin*, 1958, v. 33, 991] while cell walls of strain 569 and of the other phage-sensitive strains consist of glucose, glucosamine and another unknown hexosamine.

Janice Taverne

GÁSPÁR, Georgina. **Studies of a *Cl. perfringens* Phage. II. The Latent Period of its Growth Curve.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 3, 269–76, 4 figs.

One-step growth curves of phage 808/3a growing in *Clostridium welchii* showed that it had a latent period of 47 minutes and that during the latent period the number of infective particles slowly but definitely increased. When phage multiplication was stopped at different times by aerating infected bacteria (which were, of course, growing anaerobically) it was found that up to 25 minutes after infection, aeration caused the number of infective particles to decline, at 35 minutes the

number of particles remained constant, and after 35 minutes the number of particles increased almost as much as when the culture was incubated anaerobically. If infected cultures were incubated aerobically immediately after adsorption, then the latent period was prolonged and the number of particles did not increase during it. Incubating either phage or bacteria aerobically before adsorption did not alter the growth curve of the phage.

The author argues that the phage displays a true latent period since no phage increase is observed if infected cultures are aerated up to 35 minutes after infection. She suggests that the increase in the number of phage particles observed as early as 10 minutes after infection, when cultures are growing anaerobically, can be explained if the bacteria grow in short chains and each chain only gives rise to 1 plaque. Bubbling nitrogen into the culture would gradually disrupt the chains and individual infected cells could then each give rise to a plaque.

[For the first part of this study, see this *Bulletin*, 1960, v. 35, 508.] *Janice Taverne*

GUBA, F. & VANDRA, Edith. **An Electron Microscopic Study of *Mycobacterium* Phages.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 4, 337–40, 5 figs. [11 refs.]

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

MCCREA, J. F., EPSTEIN, R. S. & BARRY, W. H. **Use of Potassium Tartrate for Equilibrium Density-Gradient Centrifugation of Animal Viruses.** [Correspondence.] *Nature.* 1961, Jan. 21, v. 189, 220–21.

Density gradients of neutral potassium tartrate were prepared ranging from 2–35% to 2–60%. Virus was placed on top and the whole centrifuged for 1–2 hours in the Spinco SW39 head at 39,000 r.p.m. Fractions were collected by (a) running in 70% salt from below, (b) running out the contents of the tube from below, or (c) freezing the tube and sawing it up. [Method (c) is described as novel but a very similar technique is mentioned by MELNICK *et al.* (this *Bulletin*, 1952, v. 27, 210).] Sharp equilibrium peaks were obtained; in the example given, influenza A, most of the virus was found in one fraction. The authors comment on the possible scope of the method and its advantages over the use of heavy metal chlorides such as rubidium and caesium.
D. A. J. Tyrrell

CANTELL, K. **Production and Action of Interferon in HeLa Cells.** *Arch. f.d. gesamte Virusforschung.* 1961, v. 10, No. 4, 510–21, 4 figs. [30 refs.]

The Enders strain of mumps virus was added to cultures of HeLa cells. 24 hours later the cultures were challenged with poliovirus. The cytopathic effect and the yield of poliovirus were reduced in the pretreated cultures. Active virus did not produce this interference effect but virus inactivated by heating at 35°C. for 9–12 days, or by UV light did so. It was shown that HeLa cell cultures inoculated with irradiated mumps virus produced interferon, which could be detected in the medium, and which would prevent the growth of poliovirus when added to HeLa cell cultures. Unlike the mumps virus used to produce it this interferon was inactivated by trypsin but was unaffected by ultracentrifugation, absorption with red cells and treatment with antimumps virus immune serum. Interferons produced in human amnion and in HeLa cells both protected HeLa cells to the same extent.
D. A. J. Tyrrell

COHEN, E. P. & EAGLE, H. **A Simplified Chemostat for the Growth of Mammalian Cells: Characteristics of Cell Growth in Continuous Culture.** *J. Exper. Med.* 1961, Feb. 1, v. 113, No. 2, 467–74, 5 figs. [10 refs.]

BADER, J. P. & MORGAN, H. R. **Latent Viral Infection of Cells in Tissue Culture. VII. Role of Water-Soluble Vitamins in Psittacosis Virus Propagation in L Cells.** *J. Exper. Med.* 1961, Feb. 1, v. 113, No. 2, 271–81, 5 figs. [11 refs.]

In these experiments mouse fibroblasts, which had been depleted of their nutritional reserves by being maintained in Earle's balanced saline solution for 48 hours, were then grown in a synthetic medium deficient in a single water-soluble vitamin. After an extended period of growth the depleted cells were infected and the cultures maintained in the deficient medium; controls received the complete synthetic medium. Virus multiplication was followed by titration of the tissue culture fluids in the yolk sacs of 7-day embryonated eggs. In turn, the necessity of the various water-soluble vitamins for virus multiplication was investigated. And although of these vitamins pantothenate, niacin, pyridoxine and choline were necessary for maximal growth of psittacosis virus, it was thiamine, alone, which was essential to virus multiplication.

[See also this *Bulletin*, 1957, v. 32, 1206.]
S. P. Bedson

BERNKOPF, H., MASHIAH, P. & MAYTHAR, B. **Cultivation of a Strain of Trachoma Virus in the FL Line of Human Amnion Cells.** *Bull. Res. Counc. of Israel.* 1960, Nov., v. 8E, No. 4, 121–7, 9 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 746.]

NIZAMUDDIN, M. & DUMBELL, K. R. **A Simple Laboratory Test to distinguish the Virus of Smallpox from that of Alastrim.** *Lancet.* 1961, Jan. 14, 68–9. [23 refs.]

Strains of smallpox virus after inoculation to chick embryo chorioallantoic membrane produced pocks not only at 35°C. but also (in not greatly diminished numbers), at 38·25°C. Strains of alastrim virus incubated under the same conditions, however, failed uniformly to produce any pocks at 38·25°C. The authors suggest this difference in temperature sensitivity as a basis for distinguishing between strains of smallpox and alastrim viruses. On the strength of this test, a virus strain formerly thought to be smallpox was relabelled alastrim. *Colin Kaplan*

MIKA, L. A. & PIRSCH, J. B. **Differentiation of Variola from other Members of the Poxvirus Group by the Plaque Technique.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 861–3, 1 fig.

3 strains of vaccinia virus, 2 of cowpox and 1 each of rabbit pox and monkey pox viruses all produced plaques in monolayers of chick embryo cells, as well as pocks in chick embryo chorio-allantoic membranes. 13 strains of variola virus and 1 of alastrim produced pocks in the chorio-allantoic membrane, but even on repeated tests, no plaques in monolayers. Within strains, the morphology of the plaques produced was sufficiently uniform for it to be used in differentiating one strain from another.

[See also this *Bulletin*, 1960, v. 35, 707.]
Colin Kaplan

PLÁCIDO DE SOUSA, C. & FERREIRA, J. F. D. **Multiplication of Herpes Virus in a Mouse Mammary Tumor.** *Arch f.d. gesamte Virusforschung.* 1961, v. 10, No. 4, 465–77, 6 figs. [30 refs.]

Cells from a mammary tumour occurring spontaneously in a line of mice were examined microscopically and found to resemble cells from tumours caused by the Bittner agent. Oval inclusions were present in a proportion of the cells, and under the electron microscope these were seen to be composed of groups of particles of 65 $m\mu$ diameter which, outside the cell, appeared to have a dense core and a double membrane.

Herpes simplex virus inoculated into the mass of the tumour was shown to multiply locally without producing any symptoms of infection in the mice or causing the tumour to regress. Cells from infected tumours contained typical intranuclear inclusions, and, under the electron microscope, they were found to resemble chick chorio-allantoic cells infected with herpes as described by MORGAN *et al.* [this *Bulletin*, 1955, v. 30, 179]. The nucleus showed characteristic changes and contained particles of 130 $m\mu$ diameter, each with a dense core and a distinct membrane, and occasionally particles of the same size but with a double membrane were seen in the cytoplasm of such cells.

Inoculated tumours contained cells with characteristic 65 $m\mu$ cytoplasmic particles in the same frequency as uninoculated tumours. In spite of an extensive search, the authors only found 1 cell which contained both kinds of particles, in its nucleus the larger ones typical of herpes infection and in its cytoplasm the smaller ones typical of the tumour. From chance alone, they expected to observe many more such cells. They therefore conclude that the presence of the tumour agent in a cell prevents herpes virus multiplying in that cell.
Janice Taverne

SCOTT, R. F. MCN., MCLEOD, D. L. & TOKUMARU, T. **A Biologic Comparison of Two Strains of *Herpesvirus hominis*.** *J. Immunology.* 1961, Jan., v. 86, No. 1, 1–12, 8 figs. [37 refs.]

The properties of a strain of herpes simplex virus which caused syncytial giant cell formation in tissue culture have been compared with those of a strain which caused proliferative changes and rounding and piling up of cells but no syncytia [this *Bulletin*, 1958, v. 33, 1091]. Each strain caused these characteristic cytopathic changes in culture of HeLa, rabbit kidney, human amnion and chick embryo cells. The only other differences found between the strains was that infected rabbit kidney (RK) cells, up to 6 hours after infection, exhibited different hexokinase activities in each case. Otherwise, growth curves in RK cells were identical, there were no significant differences in rates of adsorption and penetration, and there were no differences in the glucose-6-phosphate dehydrogenase activity of the infected cells. Heat and UV inactivation curves were similar. Pocks on the chick chorio-allantoic membrane were indistinguishable. Both strains were equally pathogenic for mice and rabbits. No differences could be seen under the electron microscope. Finally, the strains were serologically identical in serum neutralization tests.
Janice Taverne

FELTON, Frances G. & SCOTT, L. V. **Studies on Hemagglutination with Herpes Simplex Virus. II. Factors involved in the Technique.** *J. Immunology.* 1961, Jan., v. 86, No. 1, 42–9, 2 figs.

The authors have investigated the conditions affecting the agglutination by immune serum of tanned red cells sensitized with the HF strain of herpes simplex virus derived from allantoic fluid. They found that they obtained the best results with virus purified by differential centrifugation and resuspended in saline buffered at *p*H 7·2. The antigen was stable, lasting at least 8 months at 4°C., and could be preserved with formalin or merthiolate [thiomersal]. The test was most satisfactory when sheep red cells were used. Optimally, they

were treated with a 1:20,000 concentration of tannic acid, sensitized with virus at *p*H 6·4 for 10–60 minutes at room temperature, washed, and resuspended in a diluent contining 1:100 normal rabbit serum. Antiserum dilutions were mixed with the sensitized red cells (the size of the tube did not matter) and the mixtures were left for 4 hours at room temperature or overnight at 4°C. before they were read.

[For Part I, see this *Bulletin*, 1958, v. 33, 1091.]

Janice Taverne

CHU, Liang-Wei & WARREN, G. H. **Pathogenicity and Immunogenicity Herpes Simplex Virus Strains propagated in Rabbit Kidney Tissue.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 396–9. [14 refs.]

4 strains of herpes simplex virus produced different cytopathic effects in rabbit kidney tissue cultures. Strain HF formed giant cells, strain 1166 caused the cells to clump and strains 1266 and L4 caused rounding and ballooning of cells as well as clumping. All the strains formed pocks on the chick chorioallantoic membrane and all grew as well in suckling mice as in rabbit kidney cultures. The virulence of the strains for different laboratory animals and for species of monkey varied. For instance, with adult mice injected intracerebrally 10^7 TCD50 of strain 1166 was not lethal while about 10^8 TCD50 of the other 3 strains invariably killed the mice. Strain 1166, which had been isolated from a case of aseptic meningitis and had gone through 31 egg passages, showed no cross-neutralization with the other 3 strains, which were themselves antigenically indistinguishable, nor was it neutralized by antiserum to virus B.

All the strains were found to be more potent antigenically when grown in rabbit kidney cells than in other systems in that they were more effective in mouse protection tests and, after inactivation by formalin, they induced the production of higher antibody titres in guineapigs.

Janice Taverne

HANIG, M. & STEIM, J. M. **The Difference in Effective Hydrodynamic Diameters of "Fast" and "Slow" Influenza Viruses propagated in De-Embryonated Eggs.** *Virology.* New York. 1960, Dec., v. 12, No. 4, 499–510, 1 fig. [23 refs.]

This is a report of further determinations of hydrodynamic data on "slow" (or incomplete) and "fast" (or complete) influenza virus [see HANIG and STEIM, this *Bulletin*, 1960, v. 35, 1143]. Purified "slow" and "fast" forms of PR8 virus were prepared by adsorption elution on erythrocytes and differential ultracentrifugation. Virus was sedimented in sucrose solutions of varying density and a linear relation was found between the sedimentation coefficient and the density of the solution; on extrapolation to zero the lines for both components gave the same value for the hydrated density, namely 1·18 gm. $ml.^{-1}$. Other relevant data are also given and it is concluded that the differences in sedimentation behaviour of the 2 forms are due to differences in the effective hydrated diameters, 79·3 or 84 $m\mu$ for the "fast" component and 72·7 or 79·3 $m\mu$ for the "slow".

D. A. J. Tyrrell

STEWART, R. B. & MORGAN, H. R. **Studies on Cytotropism in Animal Viruses. II. A Comparison of the Growth of Four Influenza Virus Strains *in vivo* and *in vitro* in Hatched Chick and Chick Embryo Lung Tissue.** *J. Immunology.* 1960, Nov., v. 85, No. 5, 465–8, 3 figs.

These studies [see also this *Bulletin*, 1959, v. 34, 829] were undertaken to determine some of the factors in the resistance of hatched chicks to infection with influenza virus. Virus multiplied in the lungs of 18-day-old chick embryos after inoculation of virus into the allantoic sac; virus disappeared after hatching. The Lee strain disappeared most rapidly, followed by WS and NWS and the PR8 strain least rapidly. A similar pattern of virus disappearance was seen when 2-day-old hatched chicks were inoculated intratracheally; in this experiment only the PR 8 strain appeared to multiply. These experiments showed that lung tissue of hatched chicks was relatively insusceptible, regardless of whether virus was introduced before or after hatching, and that the insusceptibility varied with the strain of virus used. However, in tissue culture at 37°C. the 4 strains of virus multiplied not only in chick embryo lung cells but also in hatched chick lung cells; but at 41°C. only strains PR8 and NWS grew. This suggested that the hatched chick body temperature of 41°C. was the reason for the failure of the Lee and WS strains to grow in the lungs of such birds. It seemed, however, that some other explanation was required for the failure to infect hatched chicks with the NWS strain of influenza virus.

D. Taylor-Robinson

HOLLÓS, I. **Inhibition of the Multiplication of Influenza Virus by Francis Inhibitor coupled to Aniline Derivatives.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 3, 231–42, 5 figs. [Numerous refs.]

Francis (or α) inhibitor was prepared from human blood plasma and coupled to various aniline derivates. It was found that when certain coupled inhibitors were mixed with influenza viruses they combined with the virus which could not be recovered from the mixture by adsorption to red cells in spite of prolonged incubation at room temperatures. When such coupled inhibitors were added to cultures of chick embryo cells they inhibited the multiplication of influenza viruses added to the cultures. The results are summarized in charts and tables [see also Hollós, *Nature*, 1961, v. 189, 553]. A/Singapore 1/57 was less susceptible than Lee, PR8 and A/Budapest 4/49. The 3 most active materials had been coupled with p-ethylaniline, diethyl-p-phenylenediamine and o-methyl aniline. Some further experiments were done with inhibitor coupled with diethyl-p-phenylene-diamine. It was shown that serum antibody was destroyed under the conditions used in preparing the inhibitors and that when the inhibitor had been

mixed with the virus it could be sedimented with the virus in the ultra centrifuge and was presumably attached to the virus particles. Also some preliminary experiments indicated that treatment of embryonated eggs or mice with coupled inhibitor reduced the yield of virus. *D. A. J. Tyrrell*

VERVILLE, E., CONNOR, J. D. & SIGEL, M. M. **Double Infection of Tissue Culture Cells with CA Virus and Adenovirus.** *Virology*. New York. 1961, Feb., v. 13, No. 2, 260–62, 1 fig. [13 refs.]

BOYER, Georgianna S., DENNY, F. W., Jr., MILLER, I. & GINSBERG, H. S. **Correlation of Production of Infectious Virus with Sequential Stages of Cytologic Alteration in HeLa Cells infected with Adenoviruses Types 5 and 7.** *J. Exper. Med.* 1960, Nov. 1, v. 112, No. 5, 865–82, 10 figs. [15 refs.]

Experiments were designed to correlate the stages of adenovirus type 5 and 7 cytopathic change with production of infectious virus in HeLa cells. 7×10^4 cells infected with $10^{5 \cdot 25}$ TCD50 of type 5 adenovirus developed nuclear changes before the appearance of intracellular infectious virus. Thus at 12 hours, 8% of the cells revealed nuclear alterations but no new virus was detectable and the sequential early nuclear stages 1 (16 hours) and 2 (18 hours) [see BOYER *et al.*, this *Bulletin*, 1960, v. 35, 313] did not appear to be associated with the production of infectious virus. Virus replication increased rapidly at 22 hours and was maximal at 24 hours when nuclear stages 3 and 4 were becoming predominant. With a smaller virus inoculum, 7×10^4 cells infected with 10^4 TCD50, the results were quantitatively but not qualitatively different, and the development of infectious virus showed the same relationship to the progression of cellular changes. Thus cytological changes preceded the detection of newly formed infectious virus; cells in stage 1 appeared to lack infectious virus whereas stage 4 was associated with the largest amounts of virus per cell.

Type 7 adenovirus was less suitable for study because the differences between the stages of nuclear change were not as well defined. Again, however, the development of the early nuclear changes (stages 1 and 2) in the majority of cells preceded the appearance of most of the mature infectious virus. *D. Taylor-Robinson*

TYRRELL, D. A. J. & BYNOE, M. L. **Some Further Virus Isolations from Common Colds.** *Brit. Med. J.* 1961, Feb. 11, 393–72, 2 figs.

The isolation of more viruses from patients with common colds is described. These viruses have required the "common cold conditions" previously described [TYRRELL *et al.*, this *Bulletin*, 1960, v. 36, 616], at least for optimal cytopathic effects. These conditions are low *p*H, low temperature and rolled cultures, preferably of human embryo kidney cells but also, for some strains, monkey kidney cells and continuous cell strains. Including their first isolates, the authors have obtained 25 viruses that they could propagate from a total of 110 throat washings and 40 nasal or throat swabs. Only 1 virus was isolated from a swab but the authors believe from other studies that nasal swabs are the best source of common cold virus. The typical cytopathic effects are illustrated. These changes were produced by 6 additional specimens but the capacity to produce these changes could not be serially propagated. Specimens yielding these viruses were collected in different parts of England including some collected as far back as 1951.

Volunteer studies revealed that the agents cultivated produced common colds although the incidence varied slightly, as did the clinical features, from strain to strain. Some washings produced colds in volunteers but no agents in tissue culture, demonstrating that additional technical modification will be necessary to demonstrate and grow these strains *in vitro*. Viruses could be reisolated from 19 out of 28 tests on volunteers who developed colds after virus administration and from 3 out of 25 who did not develop colds. It seems from studies with the HGP strain of cold virus that the excretion of virus in nasal and throat secretions is confined to a short period at the onset of clinical symptoms. Serological studies are as yet fragmentary. They reveal that a rise in antibodies follows infection and that several serotypes exist. Thus, a serum against HGP only neutralizes 2 other strains, both of which also grow in monkey kidney cells (Ha and PK), but none of the strains growing only in human embryo kidney cells. It seems that there are strains which grow in human embryo kidney cells which are not neutralized by FEB antisera. This serological heterogenicity may well explain the frequent recurrence of colds. *A. J. Beale*

MARMION, B. P. & GOODBURN, Gillian M. **Effect of an Organic Gold Salt on Eaton's Primary Atypical Pneumonia Agent and other Observations.** [Correspondence.] *Nature*. 1961, Jan. 21, v. 189, 247–8.

Hamsters were inoculated intranasally with the Hetter strain of the Eaton agent propagated in embryonated eggs. Some were treated with intraperitoneal injections of sodium aurothiomalate (Myocrysin). Pathological changes in the lungs were judged microscopically and macroscopically and were less in the treated animals than in untreated controls. Embryonated eggs were inoculated with the drug by the yolk sac route and with the agent by the amniotic route; there was less antigen stainable by specific fluorescent antibody in the bronchial mucosa of treated than in that of untreated embryos. These and other considerations suggested to the authors that the agent might in fact be a pleuropneumonia-like agent and they stained sections of the lungs of infected chick embryos by the intensified Giemsa method. "Minute pink coccobacilliform bodies were seen in association with bronchial epithelial cells", in the position in which antigen was demonstrated by fluorescent antibody, and such bodies were not seen in uninfected embryos. Some bodies were intracellular but most formed a compact layer on the surface of the cells.

D. A. J. Tyrrell

PATTYN, S. R. Identification selon la méthode de Lim et Benyesh-Melnick d'entérovirus isolés à Elisabethville. [**Identification by the Method of Lim and Benyesh-Melnick of Enteroviruses Isolated at Elisabethville**] *Ann. Soc. Belge de Méd. Trop.* 1960, Aug. 31, v. 40, No. 4, 675–83.

The method of LIM and BENYESH-MELNICK [this *Bulletin*, 1960, v. 35, 825] for the rapid typing of enteroviruses has been investigated. The authors used mainly 7 pools of sera, but also 11 pools in some tests. The method was found to be easy, and rapidly established the identity of enteroviruses without entailing a laborious series of neutralization tests. Rabbit and monkey antisera were satisfactory provided they were of sufficient titre. In order to identify a strain, it was necessary to have the appropriate antiserum in one of the pools and also, to prevent errors due to mixtures, to have each serum represented in at least 2, and preferably 3, pools.

A. J. Beale

KETLER, A., HINUMA, Y. & HUMMELER, K. **Dissociation of Infective Poliomyelitis Virus from Neutralizing Antibody by Fluorocarbon.** *J. Immunology.* 1961, Jan., v. 86, No. 1, 22–7, 1 fig. [11 refs.]

Poliomyelitis virus (type 1) was dissociated from antibody by homogenization of virus-serum mixtures with fluorocarbon (Freon 113). A description of the details of Freon treatment is given. Small amounts, 95–270 plaque units, could be recovered from excess antibody. The proportion of virus recoverable varied in the range 30–75%, being greater when less serum was used. Virus recovery does not depend upon denaturation of antibody since re-incubation of virus recovered with the treated serum results in re-neutralization. This finding—that virus can be dissociated from antibody—has practical as well as theoretical implications. Thus, attempts to recover virus from patients are often frustrated by antibody and a means for overcoming this difficulty is now at hand.

[For a preliminary study, see this *Bulletin*, 1959, v. 34, 98.] *A. J. Beale*

FRENCH, R. C., MOREAU, P. & YAROSH, W. **The Rapid Production of Antisera against Attenuated Polioviruses.** *Canadian J. Microbiol.* Ottawa. 1960, Dec., v. 6, No. 6, 599–603.

In testing attenuated poliovaccine prepared in monkey kidney cells for extraneous simian viruses, high-titre antisera capable of inhibiting undiluted poliomyelitis virus are required. Moreover, these antisera must be prepared from virus not grown in monkey kidney cells. Such sera have not in the past proved easy to prepare. It was found that high titres (10^7–10^8 PFU per ml.) of all 3 types of attenuated poliomyelitis virus could be prepared in human kidney cell cultures. These virus suspensions were inoculated intravenously into rabbits (2 ml.) or roosters (1 ml.). Each animal received a primary course of 3 injections followed by a booster 3 weeks after the primary course ended; a second booster was given 3 weeks after the first. Animals were bled 1 week after the primary and booster courses. After the first booster dose, titres of the pooled antisera were 1/3,000–1/11,000 for rabbit sera and 1/10,000–1/22,000 for rooster sera; the authors used the plaque reduction technique of serum neutralization previously described [FRENCH *et al.*, this *Bulletin*, 1960, v. 35, 316]. Roosters gave particularly good type 3 antisera. The sera were found to inhibit equal volumes of undiluted attenuated poliomyelitis virus after 2 hours at 37°C. as judged by exposure to monkey kidney cells for 14 days.

A. J. Beale

DUNNEBACKE, T. H. & MATTERN, C. F. T. **Adaptation of Coxsackie Virus Strain A-10 to Human Amnion Cells in Tissue Culture.** *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 553–4.

A strain of Coxsackie A 10 was successfully adapted to grow on primary human amnion cells. It could not be adapted to grow on HeLa cells or a series of cell lines derived from human amnion. The adapted line was of greatly reduced pathogenicity for suckling mice. It produced cytopathic changes in amnion cells similar to those produced by poliovirus. The virus also produced plaques on human amnion cells although different batches of amnion cells varied markedly in sensitivity. Titres of 10^6 or greater were consistently obtained. The Coxsackie A 10 strain adapted to primary human amnion cells was specifically neutralized by antisera prepared against the strain virulent to suckling mice.

A. J. Beale

CONNOLLY, J. H. **Myocarditis during Coxsackie B_5 Infection.** [Memoranda.] *Brit. Med. J.* 1961, Mar. 25, 877–8, 2 figs. [11 refs.]

Report of a case.

BUCKLAND, F. E., BYNOE, M. L., ROSEN, L. & TYRRELL, D. A. J. **Inoculation of Human Volunteers with E.C.H.O. Virus Type 20.** *Brit. Med. J.* 1961, Feb. 11, 397–400, 2 figs.

ECHO 20 virus was administered to 43 volunteers under the conditions of isolation and supervision exercised at the Common Cold Research Unit. 32 were infected as judged by isolation of virus and 24 of these became clinically ill. The symptoms were mainly malaise, headache and aching limbs and 14 volunteers were febrile. The commonest respiratory symptom was sore throat which was seen in 17 volunteers. 6 had tender, enlarged cervical lymph nodes. 8 volunteers suffered from alimentary tract symptoms (distension, vomiting, nausea, diarrhoea or constipation). 20 out of the 25 patients from whom virus was isolated had 4-fold or greater antibody rises to ECHO 20 virus. The illnesses did not resemble common colds although 2 volunteers had coryza. Symptoms were much less frequent and severe in volunteers given virus or virus-serum mixtures and not yielding ECHO 20. Such illnesses were even

more rare in volunteers given control materials. Thus, 1 out of 33 developed a cold and another 6 had mild symptoms. *A. J. Beale*

Ricken, D., Dux, Rosemarie & Müller, F. Virologische und morphologische Untersuchungen zur Frage der Übertragbarkeit des virus der Hepatitis epidemica des Menschen auf die Leber des bebrüteten Hühnerembryo. **[Virological and Morphological Investigations on the Question of the Transmissibility of Human Infective Hepatitis Virus to the Liver of the Chick Embryo]** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 1, 1–14, 4 figs. [36 refs.]

Sera, blood clots and suspensions of stools from 39 patients suffering from infective hepatitis were inoculated into 317 fertile eggs on the 10th–11th day of incubation by the allantoic and amniotic routes or on the chorioallantoic membrane. After 7 days of incubation a passage was made from the embryos, and the livers were examined for the presence of histological abnormalities. Necrosis was observed in the livers of embryos which had died spontaneously, but the same appearances could be reproduced in uninoculated control embryos which were killed by exposure to a temperature of 15°C. The results obtained therefore give no reason to suppose that infective hepatitis virus can multiply in the liver of chick embryos.

D. J. Bauer

Ellem, K. A. O. & Colter, J. S. **The Interaction of Infectious Ribonucleic Acid with a Mammalian Cell Line. II. Kinetics of the Formation of Infectious Centers.** *Virology.* New York. 1960, Dec., v. 12, No. 4, 511–20, 5 figs. [12 refs.]

These experiments were carried out under the optimal conditions for the infection of L cells by Mengo RNA (ribonucleic acid): 0·7M sucrose in 0·14M NaCl—0·02M potassium phosphate, *p*H 7·3 [this *Bulletin*, 1960, v. 35, 1251]. The number of infectious centres produced in a fixed number of cells was directly proportional to the concentration of RNA present over the range of 20 μgm.—2 mgm. per ml. Different preparations containing 1 μgm. RNA per ml. gave 10·6—74·0 centres in 10^6 cells. The number of centres formed was directly proportional also to the number of cells used from 10^6—2 x 10^7 cells per ml. RNA solution. The number of centres formed was however independent of the volume of the reaction mixture over a 4-fold range. The rate of formation of centres at 37°C. was linear over the first 15 minutes but decreased rapidly thereafter. The rate was markedly dependent on temperature: the maximum number of centres was formed at 15, 40, and 60 minutes respectively at 37, 27 and 17°C. An Arrhenius plot showed that the data fell into 2 sections of different slope above and below 24°C. The temperature characteristic μ (μ/2 = apparent activation energy constant/gas constant) was 18,700 cal./mole for 25–40°C. and 33,900 cal./mole for 6–21°C. *C. E. Gordon Smith*

Rosenberger, C. R. & Shaw, C. W. **Growth of Certain Arthropod-Borne Viruses in Hamster Kidney Tissue Culture.** *Proc. Soc. Exper. Biol. & Med.* 1961, Jan., v. 106, No. 1, 223–7, 3 figs. [13 refs.]

4 Group A and 5 Group B viruses were grown in trypsinized hamster kidney cultures. The starting materials were infected mouse-brain suspensions. Virus growth of Group A was titrated in the tissue cultures, of Group B in mice. After 10–12 passages in tissue culture the viruses were identified by neutralization tests. The Group A viruses (eastern and western encephalitis, Sindbis and Mayaro) caused complete cytopathic effect within 48 hours. In Group B, St. Louis, Japanese and Murray Valley encephalitis and West Nile viruses caused cytopathic changes in about 75% of cells after 3–5 days. Murray Valley virus caused less marked changes and Ilheus produced changes in about 75% of cells in 48–56 hours. After passage, Japanese encephalitis produced the changes in 24–36 hours. The titres of mouse-brain viruses in tissue culture (5·3–9·4 log) were as high as in mice (6·8–9·7 log) but after 10 tissue culture passages except for Mayaro and Sindbis the titres in tissue culture were 1·3–4·1 log higher than in mice. Maximum titres of Group A viruses in the culture fluid were found after 16–48 hours when about 50% of the cells showed cytopathic changes: maximum titres of Group B virus were reached when 25% of cells were affected. The viruses were inactivated by 5 days at 35°C. in the culture medium without cells. The neutralization tests were straightforward except with St. Louis virus. St. Louis tissue culture virus was not neutralized in mice or tissue culture unless first passaged twice in mice. This was due to an over-estimate of the titre of St. Louis virus in tissue culture because of the presence of a contaminant micro-organism ("hamster agent")—probably the L form of a bacterium. All except one of the viruses were contaminated with this agent after tissue culture passage but it did not influence virus growth. *C. E. Gordon Smith*

Metzger, J. F., Banks, I. S., Smith, C. W. & Hoggan, M. D. **Demonstration of Venezuelan Equine Encephalomyelitis in Tissue Culture by Immunofluorescence.** *Proc. Soc. Exper. Biol. & Med.* 1961, Jan., v. 106, No. 1, 212–14, 1 fig.

A strain of Venezuelan encephalitis virus isolated in Trinidad adapted to eggs then passaged in a guineapig heart cell line was used. The antiserum was prepared in a burro (*Equus asinus*). Whole serum, globulin, and serum absorbed with tissue culture cells and acetone-dried rabbit powder were conjugated with fluorescein isothiocyanate. Infected and uninfected cells were grown on coverslips and were fixed with formalin, acetone or methyl alcohol. Material fixed with formalin could be stored at 4°C. without loss for 2 weeks but material fixed in acetone or alcohol had to be stained immediately. Best results were obtained with the whole serum or the globulin. 72 hours after infection antigen was demonstrated in all preparations but not in uninfected cultures. Specific fluorescence could be demonstrated as early as 10 hours after infection with large inocula. Unconjugated immune serum blocked over 90% of the specific fluorescence. *C. E. Gordon Smith*

NYE, E. R. & BERTRAM, D. S. **Comparison of Natural and Artificial Infection of *Aedes aegypti* L. with Semliki Forest Virus.** *Virology*. New York. 1960, Dec., v. 12, No. 4, 570–77, 1 fig. & 3 graphs.

120th mouse-passage virus was used in a laboratory colony of *Aedes aegypti*. Mosquitoes were infected either by feeding on viraemic mice or on a heated suspension of infected mouse-brain in mouse blood through a mouse skin membrane. The apparatus for this is described. Groups of 3 mosquitoes were ground up at intervals in 0·2 ml. volume per mosquito and titrated by intracerebral inoculation of mice. Transmission was tested for by feeding mosquitoes, 6–27 days after infection on suckling mice which were then observed for symptoms and death. In all cases there was a drop in virus titre from the initial level over the first 2–3 days followed by a rise to 10^3 to 10^5 LD 50 per 0·03 ml. 4–5 days after infection then a slow fall in titre. The drop in titre was always more marked in mosquitoes fed artificially than in those fed on mice and on one occasion this difference exceeded 2 log LD50. Otherwise no significant difference in titre or in transmission rate was detected between the 2 groups. *C. E. Gordon Smith*

POGODINA, V. V. **Experimental Study of the Pathogenesis of Tick-Borne Encephalitis on Alimentary Infection. I. Course of Distribution on Virus in White Mice Infected Enterally.** *Problems of Virology*. London. 1960, v. 5, No. 3, 296–303, 2 figs. [Translated from Russian.] **II. Study of Pathways of Excretion of Virus from White Mice.** *Ibid.*, 304–10, 5 figs.

I. The Fateyev strain isolated from man in the Kemerovsk region was used [? passage level]. 100 LD50 given dropwise into the mouth, or by oesophageal tube, or into the rectum of mice (8–10 gm.) caused encephalitis in 41–53% with incubation periods of 5–32 days. Mice which survived were immunized (resistance indices 141–223). Within 1 hour of oral or oesophageal infection, virus could be detected in oral mucosa, small intestine, sympathetic ganglia and submaxillary lymph nodes. After 4 hours it was also detected in large intestine, mesenteric lymph nodes, blood, salivary glands, spleen and liver. After 4 days virus could be detected in every tissue examined. Animals which had no symptoms on the 11th day had virus only in the alimentary tract and associated glands and lymph nodes. In lactating mice the titres of virus in the mammary gland followed those in the blood but were higher [? significantly]. The blood titres of lactating mice were also higher than in mice weighing 8–10 gm.

II. After oral or oesophageal infection with the Fateyev or Khab-17 strains, virus was found in the faeces within 1 hour and persisted in survivors up to 26 days. It was also irregularly detected in the urine for a similar period. Both faeces and urine were obtained by dissection at post mortem. However the shed faeces of mice sick on the 6th day after oral infection titred 4 to 5 log. The virus was identified in a neutralization test. Titres in faeces were about 4 log in the first 24 hours, fell to around 2 log 2–4 days after infection then rose to about 4 log. By the 11th day the titre had fallen to 2·7 log. Titres in kidney (2 log) and urine (0·7 log) were usually lower than in the blood. In mice inoculated intracerebrally or subcutaneously virus appeared in the faeces after 24 hours and remained throughout the period of observation. Titres as high as 5 log were found in faeces of diseased mice. In faeces collected from the cage 2·5 log of virus was found compared with 4–5 log when the mice were infected by the alimentary route. In faeces, titres of 4–5 log. dropped to 1·5–3·0 log. after 24 hours at 20–22°C. under various conditions. This paper is an important warning about the handling of the cages and excreta of mice infected with tick-borne encephalitis viruses [and possibly related viruses]. *C. E. Gordon Smith*

SALMINEN, A., RENKONEN, O. V. & RENKONEN, O. **Nature of Lipid Inhibitors of Tick-Borne Encephalitis Virus Hemagglutination. I. Inhibitory Lipids of Human Serum.** *Ann. Med. Exper. et Biol. Fenniae*. Helsinki. 1960, v. 38, No. 4, 447–55. [15 refs.] **II. Inhibitory Activity of Authentic Lipids and their Mixtures.** *Ibid.*, 456–64.

I. 4–8 units of haemagglutinin prepared by a sucrose-acetone extraction technique from the Belyanchikov strain of biphasic tick-borne encephalitis virus were used. Pooled human serum was subjected to Folch partition: 30% of the HI (haemagglutinin-inhibitor) activity of the original serum was in the chloroform phase (total lipids) and only traces in the aqueous phase. The total lipids were fractionated on silicic acid and HI activity (5–10% of original) was found only in the non-phosphatide fraction. This fraction was further fractionated and activity was found only in a fraction containing triglycerides + free fatty acids + free cholesterol but not in the individual components. When the mixture was fractionated on aluminium oxide the activity was lost but when the fractions obtained were mixed it was restored. Triglycerides + cholesterol and triglycerides + fatty acids were weakly active (1:4) but cholesterol + fatty acids strongly (1:128). The whole HI activity of the total lipids could be obtained by mixing the weakly active non-phosphatides with the inactive lecithin, sphingomyelin and lysolecithin in the proportions present in the total lipids. Free fatty acids, serum lecithins, sphingomyelins and lysolecithins are strong inhibitors only when mixed with free cholesterol but cholesterol esters and serum triglycerides were inactive even when mixed with free cholesterol.

II. Pure fatty acids and their esters, bile salts, and sterols and their esters, were non-inhibitory (1·6 millimole). Glycerophosphatides and sulphuric acid esters of long chain alcohols were non-inhibitory (0·2–0·4 millimole). Cardiolipin alone was inhibitory (2 millimoles–1:256). 4 millimoles of even-numbered saturated fatty acids from C_{12} to C_{22} were inhibitory (1:16–1:32) when mixed with 10 millimoles cholesterol: but not C_2–C_{10} or C_{24}, C_{26}. The HI activity of C_{18} acids with 0–3 double bonds mixed with cholesterol was similar. With palmitic acid mixed with cholesterol HI activity increased with concentration to a plateau (1:64) at 8 millimole and above: with increasing amounts of cholesterol a plateau is also reached. Methyl palmitate was

inactive mixed with cholesterol but sulphuric acid esters of long-chain alcohols were active when so mixed. Bile acids mixed with cholesterol were about one-quarter as active as fatty acid mixtures. Glycerophosphatide cholesterol mixtures were as active as fatty acid mixtures and cardiolipin was 8 times as active. With palmitic acid only sitosterol of 3 sterols was active in replacing cholesterol. The results suggest that acidic groups are probably essential for activity and the hydroxyl groups on cholesterol may also be involved in the combination of inhibitor and haemagglutinin.

[The concentrations of lipids are presumably expressed as millimoles, which is the term used in the text, but in the tables (and once in the text) the term μmoles is used for these concentrations; the difference would be 1000-fold.] *C. E. Gordon Smith*

TOYOSHIMA, K., FUKAI, K., HATA, S. & KUNITA, N. **Concentration of Measles Virus and its Complement Fixing Antigen.** [Correspondence.] *Biken's J.* Osaka. 1960, Mar., v. 3, No. 1, 133–4.

The Toyoshima strain of measles virus multiplies well in cultures of FL cells and titres of 10^6 TCD50 per 0·2 ml. can be obtained in the culture fluid. In the present work the concentration of virus and soluble antigen by means of centrifugation for 90 minutes in fields ranging from 1,650 to 53,800 *g* has been studied. A rise in virus titre from 6·3 log units per 0·2 ml. in the initial culture fluid to 6·8 log units in the resuspended sediment was achieved by centrifugation at 1,650 *g* and no greater concentration was obtained with the higher gravitational fields. An 8-fold increase in titre of complement-fixing antigen was observed at the same time. *D. J. Bauer*

SERGIEV, P. G., RYAZANTSEVA, N. E. & SHROIT, I. G. **The Dynamics of Pathological Processes in Experimental Measles in Monkeys.** *Acta Virologica.* Prague. 1960, Sept., v. 4, No. 5, 265–73, 2 text-figs. & 10 figs. on 5 pls. [18 refs.]

The authors have studied the relationship between multiplication of virus and development of lesions in 14 monkeys (*Papio hamadryas* and *P. hybridus*) infected with measles virus (4 with blood from a child in the prodromal stage, and 10 from these 4 in a similar stage) subcutaneously, orally, intranasally and on the conjunctiva and killed for examination at intervals up to 17 days after infection. The content of virus in the blood, skin, mucous membranes and internal organs was determined by the AVB test [agglutination of virus adsorbed on bacteria; (Sergiev *et al., Zh. Microbiol. Epidemiol. Immunol.,* 1945, No. 3, 14)] and the tissues were examined histologically. From the results obtained it was possible to distinguish 3 phases in the pathogenesis of the experimental infection. (1) 1st–6th day; moderate viraemia with multiplication of the virus in the lymphoid tissues. (2) 6th–11th day; more marked viraemia with leucopenia and prodromal symptoms; giant cells appear in the lymphoid tissues. (3) 9th–11th day onwards; a maculopapular rash appears and the viraemia passes off; the characteristic lesions in the lymphoid tissues gradually disappear. *D. J. Bauer*

WILLIAMS, M. G., HOWATSON, A. F. & ALMEIDA, J. D. **Morphological Characterization of the Virus of the Human Common Wart (*Verruca vulgaris*).** *Nature.* 1961, Mar. 18, v. 189, 895–7, 3 figs.

NICOLAU, S. S., DRĂGĂNESCU, N., NICOLAU, C., IONESCU, N. I., FUHRER, B. & GÎRD, E. **Experimental Researches on "Silvered" Anti-Rabies Vaccine.** *Rev. Sci. Méd.* Bucharest. 1959, v. 4, 81–4. [10 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1961, v. 58, 683.]

IMMUNITY

DINEEN, J. K. & PERRY, B. T. **Studies on the Nature of Antibody Production during the *in vitro* Culture of Lymphoid Tissues.** *Australian J. Exper. Biol. & Med. Sci.* 1960, Oct., v. 38, Pt. 5, 363–74. [19 refs.]

"A simple and reproducible technique for the study of the production of antibodies by lymphoid tissues during *in vitro* culture has been described.

"Cellular and extra-cellular fluid titres were estimated by Boyden's tanned cell technique, and a sharp rise in the fluid antibody titre (up to 300-fold) was observed during the first 18 to 24 hours of culture, while the cellular titre remained at a low constant level. The results of this study suggest that antibody-producing cells store little or no classical antibody.

"The presence of chloramphenicol in the culture medium inhibited antibody production, while production was not specifically inhibited by ribonuclease. In addition, antibody production was inhibited by the absence of Ca++ from the culture medium and this effect was reversed when Ca++ was restored in physiological concentration.

"Attempts to stimulate antigenically spleen and popliteal node tissues during *in vitro* cultures were not successful."

DINEEN, J. K. & PERRY, B. T. **The Immunological Response produced in Inbred Mice following the Isologous and Homologous Transfer of Antigenically Stimulated Spleen Cells.** *Australian J. Exper. Biol. & Med. Sci.* 1960, Oct., v. 38, Pt. 5, 375–87, 1 fig. [12 refs.]

"Antigenically stimulated spleen cells from C3H and C57Bl mice have been transferred to isologous and

homologous recipients and both the immediate appearance of antibody and the response to a challenge injection of antigen 11–12 weeks later have been studied.

"Antibody can be detected as early as two days after isologous transfer of C57Bl cells, but none appears after homologous transfer. Isologous transfer of C3H cells gives much less evidence of early response showing either a delay up to six days before first appearance or failing completely.

"Following late challenge mice that received isologous cells responded with typical secondary response in the great majority. No secondary type responses were obtained with homologous combinations."

BISHOP, D. W. & GUMP, D. **Production of Circulating Antibody against Defined Antigen (BCG) by Neonatal Guinea Pigs.** *Proc. Soc. Exper. Biol. & Med.* 1961, Jan., v. 106, No. 1, 24–7, 1 fig. [13 refs.]

"Neonatal guinea pigs, injected with BGG and adjuvant immediately after birth produce circulating antibody, detectable by PCA but not by agar-diffusion tests. Sera collected 7, 9, 11, and 15 days after intramuscular injection gave 7, 80, 94, and 100% positive PCA reactions, respectively. Rate of antibody production during the first week after birth is lower than that of adults. Capacity for humoral antibody formation probably exists at a reduced level in the fetus."

PATTERSON, R., WEIGLE, W. O. & DIXON, F. J. **Elimination of Circulating Serum Protein Antigens as a Sensitive Measure of Antibody.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 330–35, 3 figs. [17 refs.]

The production of antibody after injection of soluble serum protein antigens into animals can readily be detected by the rapid elimination of the antigen from the circulation of the sensitized animal. The rate of elimination depends on the amount of antigen injected, the rate of antibody formation and perhaps the quality of antibody produced. The purpose of the present investigation was to determine the minimum amount of passively transferred antibody which could be detected by the rapid elimination of antigen labelled with ^{131}I. Working with passively immunized rabbits and rabbits, mice and guineapigs injected with antigen-antibody complexes labelled with ^{131}I, the authors detected levels of antibody as low as 0·0012–0·0033 μgm. antibody N per ml. of plasma, showing that the sensitivity of this immune elimination of antigen technique compares favourably with other methods of detecting antibody. The method cannot be used, however, to make an absolute quantitative estimation of antibody. These findings are discussed in relation to the natural selection theories of antibody formation. *D. A. Cannon*

MIYA, F., MARCUS, S. & PERKINS, E. H. **The Properdin System in Mice.** *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 668–71. [17 refs.]

The properdin system comprises properdin, magnesium ions and all 4 components of complement. Normal mouse serum has a high properdin level but no bactericidal activity. As it is known that mouse serum is deficient in one or more components of complement, the authors carried out experiments to see whether (a) parenteral injection of complement into the mouse might alter the animal's ability to withstand bacterial infection, and (b) addition of complement to mouse serum might result in bactericidal activity *in vitro*. Both sets of experiments ended in failure: the results obtained contributed no evidence to support the suggested importance of the properdin system, but the discussion gives reasons why the data presented cannot be taken as definite evidence that the properdin system is not significant in the natural defences of the mouse.

D. A. Cannon

KORNFELD, Lottie & MILLER, C. P. **Restoration of Serum Bactericidal Activity and Prevention of its Loss in X-Irradiated Mice.** *J. Immunology.* 1961, Feb., v. 86, No. 2, 215–19. [10 refs.]

"1. The loss of normal serum bactericidal activity of CF-1 mice for a strain of *Escherichia coli* which occurs 12 hr after total-body x-irradiation (600 r) was prevented if yeast autolysate, yeast ribonucleic acid, homogenates of normal mouse spleens or bacterial endotoxin were injected ½ hr before or ½ hr after exposure to x-rays. Injection 18 hr before irradiation was without effect.

"2. Injection of any of these substances during the postirradiation period, when bactericidal activity was absent, resulted in the appearance of bactericidins 18 hr after treatment.

"3. Spleens removed from donor mice 1 or more hours after exposure to 600 r failed to restore bactericidins in irradiated recipients."

HOWARD, J. G. **The Reticulo-Endothelial System and Resistance to Bacterial Infection.** *Scottish Med. J.* Glasgow. 1961, Feb., v. 6, No. 2, 60–82. [Numerous refs.]

A review of the subject.

WARWICK, W. J., ARCHER, Olga & GOOD, R. A. **Passive Transfer of Delayed Sensitivity to the Newborn Rabbit.** *Proc. Soc. Exper. Biol. & Med.* 1960, Dec,. v. 105, No. 3, 459–61, 1 fig.

Delayed sensitivity was induced by infecting adult rabbits with the Dematteo strain of streptococcus. 7–10 days after infection the animals were skin-tested for sensitivity by the intradermal injection of 0·01 ml. normal saline containing 100 units of streptokinase and 3·3 units of streptodornase (Varidase): grades of induration and erythema were numbered 0 to 5. From the spleens and popliteal nodes of rabbits showing a positive skin test, leucocytes were obtained by dissection, sieving and centrifugation, and after resuspension in saline were injected—intravenously, subcutaneously and intraperitoneally—into newborn rabbits and mature control rabbits, which were subsequently skin-tested with streptokinase (1,000 units) and streptodornase (33 units). The results show that the newborn rabbit, like the newborn human infant, is unable to accept the passive transfer of delayed sensitivity: the ability to do this develops about the age of 4 weeks. *D. A. Cannon*

Miscellaneous

KAPLAN, E. & SHAULL, R. S. **Determination of Lead in Paint Scrapings as an Aid in the Control of Lead Paint Poisoning in Young Children.** *Amer. J. Pub. Health.* 1961, Jan., v. 51, No. 1, 65–9, 1 fig. [12 refs.]

The frequency of lead intoxication in children from the ingestion of scaling or peeling paint on surfaces in the home [this *Bulletin,* 1959, v. 34, 785, 849; 1960, 1157] reported particularly from some cities in the United States has led to action being taken by public health authorities. Among the health ordinances now adopted by some health authorities is the ordinance that prohibits the use for interior painting of paint that is not free of lead pigment. Also, warning labels must be affixed to any paint containing more than 1% of lead determined as metallic lead based on the total non-volatile content of the paint.

Testing of paint is therefore necessary to enforce the labelling ordinance but the methods for the determination of lead in paint at the 1% level are long and tedious.

In this paper there is a description of a practical screening test, suitable for the laboratory and in the field which requires only 25 mgm. of a sample of paint scrapings. It does not make a true quantitative determination but is claimed to give a positive result in a very short time if the lead concentration is over 1%. Particulars are given with a diagram of making a field balance, capable of weighing 25 mgm. of paint scrapings, out of plain white index card glued to a piece of balsa wood. The weighed sample transferred to a Pyrex tube is treated with 3 drops of nitric acid solution, followed after 15 minutes in a boiling water bath (in a fume cupboard), by 2 ml. of 1% sodium sulphite solution. It is centrifuged, then kept in a water bath at 60–65°F. for 5 minutes after which 2 drops of a 20% solution of potassium iodide are added. If more than 1% of lead is present in the paint an immediate yellow precipitate will appear. *M. E. Delafield*

SHRAND, H. **Treatment of Lead Poisoning with Intramuscular Edathamil Calcium-Disodium.** *Lancet.* 1961, Feb. 11, 310–12. [25 refs.]

This is a short and interesting paper in which much of the recent literature on lead poisoning in children is reviewed [this *Bulletin,* 1952, v. 28, 33; 1956, v. 31, 980; 1957, v. 32, 302, 548; 1959, v. 34, 722; 1960, v. 35, 969]. In most of such cases a history of pica can be obtained on questioning but many parents regard the habit as a part of the teething stage. Lead poisoning in children is prevalent in North America but only about 30 cases have been reported in Great Britain in recent years although it is obvious that many more have not been reported.

"The average toddler takes about three months to nibble away enough lead-containing paint to produce symptoms." The symptoms are described with stress on those indicating encephalopathy which has a mortality of about 25% and among the survivors an extremely high incidence of permanent mental sequelae [*ibid.,* 1955, v. 30, 734; 1959, v. 34, 849].

Lead poisoning must be diagnosed early and should be suspected in all cases of pica whether there are symptoms or not. The diagnosis is established by finding a blood-level above 50 μgm. per 100 gm. of blood and a 24-hour urinary lead excretion above 80 μgm. per litre. These tests take time and need special lead-free apparatus. A table is given of screening aids and tests found to be useful in making a presumptive diagnosis which include (1) pica history, (2) X-ray of abdomen and long bones, (3) glycosuria, (4) basophilic stippling, (5) coproporphyrinuria and (6) urinary δ-amino-laevulic acid.

The main purpose of this paper is to illustrate by case reports of lead poisoning in 2 children, aged 16 months and 2 years, the value in treatment of edathamil calcium disodium given intramuscularly instead of by the intravenous or subcutaneous routes which have great disadvantages. Edathamil as a 5% solution with 0·5% procaine and 0·5% chlorcresol was injected intramuscularly into the buttock twice or more times a day at a total daily dose of the drug of 35 mgm. per kgm. of body weight in 1 patient but 75 mgm. in the severer case. Treatment was continued for 5 days. The injections caused no local reaction or pain, were followed by rapid clinical improvement and in the milder case were carried out at home. *M. E. Delafield*

SCHAFIR, M. **The Management of Acute Poisoning by Ferrous Sulfate.** *Pediatrics.* Springfield, Ill. 1961, Jan., v. 27, No. 1, 83–94. [47 refs.]

"A review of the medical literature of the last 13 years reveals an increasing awareness by physicians and a seemingly increasing incidence of acute ferrous sulfate poisoning. The mortality rate has been about 50%." The source of the poison is usually iron preparations prescribed for adults, mostly for pregnant women, and the children most commonly poisoned are toddlers.

Case reports are presented here of poisonings in 2 children aged 15 and 16 months, 1 of which was extremely severe. Both children had ingested large amounts of ferrous sulphate. Treatment was by edathamil along with other therapeutic measures and both children recovered completely. The course of the poisonings, the clinical features and the results of extensive studies of the blood corpuscles and serum, the urine and the gastrointestinal tract are described.

The pathophysiology of acute iron poisoning and its therapy particularly that by edathamil are fully discussed in the light of the literature with emphasis on the gaps in knowledge of these subjects.

A long outline is given of the recommended procedures in treatment which to be successful must be "immediate, vigorous and sustained."

It is realized that in this therapeutic regimen "many facets need further elucidation". On the evidence of these 2 cases edathamil would appear to have "potential

usefulness" when used in conjunction with other essential procedures which include treatment of shock, maintenance of an open airway, gastric lavage and other measures. *M. E. Delafield*

CANN, H. M. & VERHULST, H. L. **Fatal Acute Chloroquine Poisoning in Children.** *Pediatrics.* Springfield, Ill. 1961, Jan., v. 27, No. 1, 95–102, 1 fig. [34 refs.]

Poisoning by chloroquine has been a rare event in the United States where malaria and amoebiasis occur infrequently. No reports of fatal poisoning in the American and British medical literature are known to the authors. The drug has, however, recently been employed in the United States in the treatment of rheumatoid arthritis and lupus erythematosis, so increasing opportunities for its accidental ingestion by young children. Reports of chloroquine poisoning have been submitted by poison control centres. Presented in this paper are accounts of 3 fatal and 1 non-fatal cases of poisoning in young children after ingestion of more than therapeutic doses of the drug. These fatal cases of chloroquine poisoning appear to be the first to be published in the English language.

In all the fatal cases death occurred about 2 hours after ingestion of chloroquine. The drug had been taken in tablet form. The amounts ingested were 0·75–1·0 gm. by a 3-year-old boy, 1·0–2·0 gm. by a 14-month-old boy and in the third case a 2-year-old boy who died and his brother aged 5 who recovered had between them consumed 3·0–3·5 gm.

In 2 of these 3 fatal cases respiratory and cardiac arrest occurred suddenly and the third fatality resulted within 30 minutes after onset of symptoms following a generalized seizure.

There is a long discussion in which there is a description of the chemistry, pharmacology and toxic effects of chloroquine, references to cases of poisoning in the medical literature of other countries and also to the mechanism of deaths from quinidine and quinine overdosage. The quinoline ring in chloroquine, quinidine and quinine may be responsible for the toxicity of all these drugs. *M. E. Delafield*

WHITTEN, C. F., KESAREE, Nirmala M. & GOODWIN, J. F. **Managing Salicylate Poisoning in Children. An Evaluation of Sodium Bicarbonate Therapy.** *Amer. J. Dis. Children.* 1961, Feb., v. 101, No. 2, 178–94. [42 refs.]

In the management of salicylate poisoning no method has been devised which will reduce the toxicity of the salicyl radical and no means of augmenting the degradation of this radical in the body is available. Therapy has therefore been directed toward effecting rapid removal of salicylates from the body and this can be effected by exchange transfusion or by dialysis. A simpler method is to make the urine alkaline—which is known to accelerate the rate of renal excretion of salicylates. This alkalinization can be obtained by the intravenous infusion of sodium bicarbonate or sodium lactate, a method about which there has been considerable controversy for an objection to the procedure has been the possible hazard of accentuating the systemic alkalosis that is a feature of the early phase of salicylate poisoning.

The purpose of the study here described was to evaluate this alkalizing therapy by sodium bicarbonate in the management of salicylate poisoning. The subjects of the study were 20 children from 4 months to 4 years of age admitted to hospital for salicylate poisoning. The material and methods of study of 18 of these 20 children are very fully described and several tables give precise details of the analytical findings.

On admission to hospital gastric lavage was performed if the accidental ingestion of salicylate had occurred within 3 hours. An indwelling catheter was inserted into the bladder and 20 to 40 ml. of 0·89 M sodium bicarbonate was infused intravenously during 5 minutes with a further infusion if the urine had not become alkaline. After this, continuous infusion with a more dilute bicarbonate solution was carried out over a longer period.

Hourly venous blood samples were examined to determine the plasma salicylate level, the percentage of salicylate bound to plasma proteins, the plasma CO_2 content, the blood *p*H and the plasma sodium and potassium concentrations. Urine samples were taken every 30 minutes to measure the volume, the *p*H and the free and total salicylate. The urinary sodium and potassium was also determined in 5 patients.

The main conclusion is that this method is as effective as exchange transfusion and dialysis for in these children whose plasma salicylate concentrations ranged from 15 to 115 mgm. %, a 50% reduction in these salicylate levels was achieved in 2–5 hours. The method of therapy is rapid and easy to apply. No toxic symptoms associated with the therapy were noted. The degree of systemic alkalosis created was not sufficient to be a contra-indication of the therapy. The importance of administering potassium in conjunction with sodium bicarbonate in certain circumstances is emphasized. The authors did not administer potassium in this study, but later they were able to prevent a significant decrease in plasma potassium levels by adding potassium to the intravenous fluid at a concentration of 30–40 m Eq. per litre. *M. E. Delafield*

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